INVENTOR SEARCH

```
=> fil capl; d que nos 116; d que nos 182;s 116,182; fil medl; d que nos 145
FILE 'CAPLUS' ENTERED AT 15:34:46 ON 19 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 19 Mar 2008  VOL 148 ISS 12
FILE LAST UPDATED: 18 Mar 2008  (20080318/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE


L1             1 SEA FILE=CAPLUS ABB=ON  US2006-565591/AP
L8               STR
L13          136 SEA FILE=REGISTRY SSS FUL L8
L14          149 SEA FILE=CAPLUS ABB=ON  L13
L15           36 SEA FILE=CAPLUS ABB=ON  KARAOLIS D?/AU
L16            9 SEA FILE=CAPLUS ABB=ON  (L1 OR L15) AND L14



L15           36 SEA FILE=CAPLUS ABB=ON  KARAOLIS D?/AU
L74           41 SEA FILE=CAPLUS ABB=ON  CYCLIC/OBI(W) DI/OBI(W)((GUANOSINE/OBI(
                 2W)(MONOPHOSPHATE/OBI OR MONO PHOSPHATE/OBI)) OR GMP/OBI)
L75           28 SEA FILE=CAPLUS ABB=ON  CYCLIC/OBI(W)(DINUCLEOTIDE/OBI OR (DI
                 NUCLEOTIDE/OBI))
L82            4 SEA FILE=CAPLUS ABB=ON  L15 AND (L74 OR L75)



L89            9 (L16 OR L82)


FILE 'MEDLINE' ENTERED AT 15:34:46 ON 19 MAR 2008

 FILE LAST UPDATED: 18 Mar 2008 (20080318/UP).  FILE COVERS 1949 TO DATE.

  MEDLINE has been updated with the National Library of Medicine's
  revised 2008 MeSH terms.  See HELP RLOAD for details.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.
```

```
L8              STR
L13         136 SEA FILE=REGISTRY SSS FUL L8
L43           2 SEA FILE=REGISTRY ABB=ON  L13 AND MEDLINE/LC
L44          79 SEA FILE=MEDLINE ABB=ON  L43
L45          17 SEA FILE=MEDLINE ABB=ON  L44 AND PY<2004


=> d que nos 147
L8              STR
L13         136 SEA FILE=REGISTRY SSS FUL L8
L43           2 SEA FILE=REGISTRY ABB=ON  L13 AND MEDLINE/LC
L44          79 SEA FILE=MEDLINE ABB=ON  L43
L46          27 SEA FILE=MEDLINE ABB=ON  KARAOLIS D?/AU
L47           6 SEA FILE=MEDLINE ABB=ON  L44 AND L46


=> fil medl agricola pascal caba wpix biotechno biosis esbio lifesci confsci
biotechds dissabs bioeng embase ; d que 173
FILE 'MEDLINE' ENTERED AT 15:35:19 ON 19 MAR 2008

FILE 'AGRICOLA' ENTERED AT 15:35:19 ON 19 MAR 2008

FILE 'PASCAL' ENTERED AT 15:35:19 ON 19 MAR 2008
Any reproduction or dissemination in part or in full,
by means of any process and on any support whatsoever
is prohibited without the prior written agreement of INIST-CNRS.
COPYRIGHT (C) 2008 INIST-CNRS. All rights reserved.

FILE 'CABA' ENTERED AT 15:35:19 ON 19 MAR 2008
COPYRIGHT (C) 2008 CAB INTERNATIONAL (CABI)

FILE 'WPIX' ENTERED AT 15:35:19 ON 19 MAR 2008
COPYRIGHT (C) 2008 THE THOMSON CORPORATION

FILE 'BIOTECHNO' ENTERED AT 15:35:19 ON 19 MAR 2008
COPYRIGHT (C) 2008 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'BIOSIS' ENTERED AT 15:35:19 ON 19 MAR 2008
Copyright (c) 2008 The Thomson Corporation

FILE 'ESBIOBASE' ENTERED AT 15:35:19 ON 19 MAR 2008
COPYRIGHT (C) 2008 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'LIFESCI' ENTERED AT 15:35:19 ON 19 MAR 2008
COPYRIGHT (C) 2008 Cambridge Scientific Abstracts (CSA)

FILE 'CONFSCI' ENTERED AT 15:35:19 ON 19 MAR 2008
COPYRIGHT (C) 2008 Cambridge Scientific Abstracts (CSA)

FILE 'BIOTECHDS' ENTERED AT 15:35:19 ON 19 MAR 2008
COPYRIGHT (C) 2008 THE THOMSON CORPORATION

FILE 'DISSABS' ENTERED AT 15:35:19 ON 19 MAR 2008
COPYRIGHT (C) 2008 ProQuest Information and Learning Company; All Rights Reserved.

FILE 'BIOENG' ENTERED AT 15:35:19 ON 19 MAR 2008
COPYRIGHT (C) 2008 Cambridge Scientific Abstracts (CSA)

FILE 'EMBASE' ENTERED AT 15:35:19 ON 19 MAR 2008
```

```
L49         184 SEA KARAOLIS D?/AU
L50         298 SEA CYCLIC(W) DI(W)((GUANOSINE(2W)(MONOPHOSPHATE OR MONO
                PHOSPHATE)) OR GMP)
L51         117 SEA CYCLIC(W)(DINUCLEOTIDE OR (DI NUCLEOTIDE))
L52       76606 SEA BIOFILM# OR BIO FILM#
L53      287453 SEA VIRULENCE
L54      304524 SEA COLONIZ? OR COLONIS?
L55      308594 SEA STAPH? AUREUS
L56       40320 SEA VIBRIO CHOLERAE
L57       23381 SEA SALMONELLA ENTERITIDIS
L58     6555431 SEA INFECT?
L59       61363 SEA MASTITIS
L60     2139386 SEA MICROB?
L61      335747 SEA ANTIMICROB?
L62      445499 SEA ANTIBACTERI?
L63     5163539 SEA BACTERI?
L64      881355 SEA IMPLANT?
L65      390178 SEA PROSTHE?
L66          30 SEA L49 AND (L50 OR L51)
L73          30 SEA L66 OR (L66 AND (L52 OR L53 OR L54 OR L55 OR L56 OR L57 OR
                L58 OR L59 OR L60 OR L61 OR L62 OR L63 OR L64 OR L65))


=> dup rem 189,147,173
FILE 'CAPLUS' ENTERED AT 15:35:48 ON 19 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'MEDLINE' ENTERED AT 15:35:48 ON 19 MAR 2008

FILE 'AGRICOLA' ENTERED AT 15:35:48 ON 19 MAR 2008

FILE 'PASCAL' ENTERED AT 15:35:48 ON 19 MAR 2008
Any reproduction or dissemination in part or in full,
by means of any process and on any support whatsoever
is prohibited without the prior written agreement of INIST-CNRS.
COPYRIGHT (C) 2008 INIST-CNRS. All rights reserved.

FILE 'WPIX' ENTERED AT 15:35:48 ON 19 MAR 2008
COPYRIGHT (C) 2008 THE THOMSON CORPORATION

FILE 'BIOSIS' ENTERED AT 15:35:48 ON 19 MAR 2008
Copyright (c) 2008 The Thomson Corporation

FILE 'ESBIOBASE' ENTERED AT 15:35:48 ON 19 MAR 2008
COPYRIGHT (C) 2008 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'LIFESCI' ENTERED AT 15:35:48 ON 19 MAR 2008
COPYRIGHT (C) 2008 Cambridge Scientific Abstracts (CSA)

FILE 'BIOTECHDS' ENTERED AT 15:35:48 ON 19 MAR 2008
COPYRIGHT (C) 2008 THE THOMSON CORPORATION

FILE 'BIOENG' ENTERED AT 15:35:48 ON 19 MAR 2008
COPYRIGHT (C) 2008 Cambridge Scientific Abstracts (CSA)
```

```
FILE 'EMBASE' ENTERED AT 15:35:48 ON 19 MAR 2008
Copyright (c) 2008 Elsevier B.V. All rights reserved.
PROCESSING COMPLETED FOR L89
PROCESSING COMPLETED FOR L47
PROCESSING COMPLETED FOR L73
L90          12 DUP REM L89 L47 L73 (33 DUPLICATES REMOVED)
                ANSWERS '1-9' FROM FILE CAPLUS
                ANSWERS '10-11' FROM FILE MEDLINE
                ANSWER '12' FROM FILE WPIX

=> d ibib abs hitind hitstr 1-9; d iall 10-11; d iall abex tech 12

L90  ANSWER 1 OF 12  CAPLUS  COPYRIGHT 2008 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2007:1122256  CAPLUS  Full-text
DOCUMENT NUMBER:          147:514687
TITLE:                    Cyclic Di-GMP stimulates
                          protective innate immunity in bacterial pneumonia
AUTHOR(S):                Karaolis, David K. R.; Newstead, Michael W.;
                          Zeng, Xianying; Hyodo, Mamoru; Hayakawa, Yoshihiro;
                          Bhan, Urvhashi; Liang, Hallie; Standiford, Theodore J.
CORPORATE SOURCE:         Intragenics Research Institute, Havre de Grace, MD,
                          21078, USA
SOURCE:                   Infection and Immunity (2007), 75(10), 4942-4950
                          CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER:                American Society for Microbiology
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Innate immunity is the primary mechanism by which extracellular bacterial
     pathogens are effectively cleared from the lung.  We have previously shown
     that cyclic di-GMP (c-di-GMP [c-diguanylate]) is a novel small mol.
     immunomodulator and immunostimulatory agent that triggers protective host
     innate immune responses.  Using a murine model of bacterial pneumonia, we show
     that local intranasal (i.n.) or systemic s.c. (s.c.) administration of c-di-
     GMP prior to intratracheal (i.t.) challenge with Klebsiella pneumoniae
     stimulates protective immunity against infection. Specifically, i.n. or s.c.
     administration of c-di-GMP 48 and 24 h prior to i.t. K. pneumoniae challenge
     resulted in significantly increased survival. Pretreatment with c-di-GMP
     resulted in a 5-fold reduction in bacterial CFU in the lung (P < 0.05) and an
     impressive > 1,000-fold decrease in CFU in the blood (P < 0.01).  C-di-GMP
     administration stimulated a robust innate response to bacterial challenge,
     characterized by enhanced accumulation of neutrophils and αβ T cells, as well
     as activated NK and αβ T lymphocytes, which was associated with earlier and
     more vigorous expression of chemokines and type I cytokines.  Moreover, lung
     macrophages recovered from Klebsiella-infected mice pretreated with c-di-GMP
     expressed greater quantities of inducible nitric oxide synthase and nitric
     oxide ex vivo than did macrophages isolated from infected mice pretreated with
     the control, c-GMP.  These findings demonstrate that c-di-GMP delivered in
     either a compartmentalized or systemic fashion stimulates protective innate
     immunity in the lung and protects mice against bacterial invasion.  We propose
     that the cyclic dinucleotide c-di-GMP may be used clin. as an effective
     immunomodulator, immune enhancer, and vaccine adjuvant to protect against
     respiratory infection and pneumonia in humans and animals.
CC   1-7 (Pharmacology)
ST   cyclic dinucleotide GMP immunomodulator
     immunostimulator innate immunity bacterial pneumonia
IT   Pneumonia
        (bacterial; cyclic Di-GMP stimulates
        protective innate immunity in bacterial pneumonia)
IT   Immunomodulators
     Immunostimulants
```

Klebsiella pneumoniae
Macrophage
Neutrophil
(cyclic Di-GMP stimulates protective innate immunity in bacterial pneumonia)

IT Interleukin 12
Macrophage inflammatory protein 2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cyclic Di-GMP stimulates protective innate immunity in bacterial pneumonia)

IT Immunity
(innate; cyclic Di-GMP stimulates protective innate immunity in bacterial pneumonia)

IT Chemokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(interferon γ-inducible protein-10; cyclic Di-GMP stimulates protective innate immunity in bacterial pneumonia)

IT T cell (lymphocyte)
(natural killer; cyclic Di-GMP stimulates protective innate immunity in bacterial pneumonia)

IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ; cyclic Di-GMP stimulates protective innate immunity in bacterial pneumonia)

IT 10102-43-9, Nitric oxide, biological studies 501433-35-8, Inducible nitric oxide synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cyclic Di-GMP stimulates protective innate immunity in bacterial pneumonia)

IT 61093-23-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclic Di-GMP stimulates protective innate immunity in bacterial pneumonia)

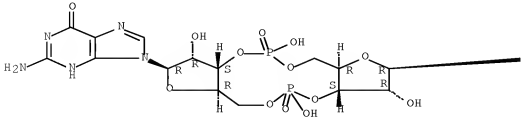
IT 61093-23-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclic Di-GMP stimulates protective innate immunity in bacterial pneumonia)

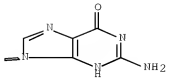
RN 61093-23-0 CAPLUS

CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L90 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2007:124392 CAPLUS Full-text
DOCUMENT NUMBER: 146:204267
TITLE: Bacterial c-di-GMP Is an Immunostimulatory Molecule
AUTHOR(S): Karaolis, David K. R.; Means, Terry K.; Yang, De; Takahashi, Munehisa; Yoshimura, Teizo; Muraille, Eric; Philpott, Dana; Schroeder, John T.; Hyodo, Mamoru; Hayakawa, Yoshihiro; Talbot, Brian G.; Brouillette, Eric; Malouin, Francois
CORPORATE SOURCE: Intragenics Research Institute, Havre de Grace, MD, 21078, USA
SOURCE: Journal of Immunology (2007), 178(4), 2171-2181
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cyclic diguanylate (c-di-GMP) is a bacterial intracellular signaling mol. The authors have shown that treatment with exogenous c-di-GMP inhibits Staphylococcus aureus infection in a mouse model. The authors now report that c-di-GMP is an immodulator and immunostimulatory mol. Intramammary treatment of mice with c-di-GMP 12 and 6 h before S. aureus challenge gave a protective effect and a 10,000-fold reduction in CFUs in tissues. I.m. vaccination of mice with c-di-GMP coinjected with S. aureus clumping factor A (ClfA) Ag produced serum with significantly higher anti-ClfA IgG Ab titers compared with ClfA alone. I.p. injection of mice with c-di-GMP activated monocyte and granulocyte recruitment. Human immature dendritic cells (DCs) cultured in the presence of c-di-GMP showed increased expression of costimulatory mols. CD80/CD86 and maturation marker CD83, increased MHC class II and cytokines and chemokines such as IL-12, IFN-γ, IL-8, MCP-1, IFN-γ-inducible protein 10, and RANTES, and altered expression of chemokine receptors including CCR1, CCR7, and CXCR4. C-di-GMP-matured DCs demonstrated enhanced T cell stimulatory activity. C-di-GMP activated p38 MAPK in human DCs and ERK phosphorylation in human macrophages. C-di-GMP is stable in human serum. The authors propose that cyclic dinucleotides like c-di-GMP can be used clin. in humans and animals as an immunomodulator, immune enhancer, immunotherapeutic, immunoprophylactic, or vaccine adjuvant.

CC 15-2 (Immunochemistry)
Section cross-reference(s): 1, 14

IT 61093-23-0, 3',5'-Cyclic diguanylic acid
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunostimulatory activity of)

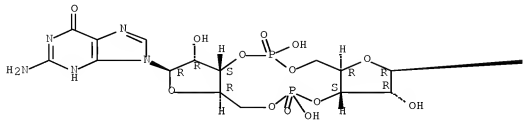
IT 61093-23-0, 3',5'-Cyclic diguanylic acid
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunostimulatory activity of)

RN 61093-23-0 CAPLUS

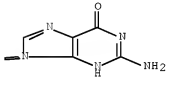
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L90 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2005:300236 CAPLUS Full-text
DOCUMENT NUMBER: 142:367640
TITLE: Method for attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs
INVENTOR(S): Karaolis, David K. R.
PATENT ASSIGNEE(S): University of Maryland, USA
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005030186	A2	20050407	WO 2004-US23498	20040722
WO 2005030186	A3	20050714		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,

SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004275696	A1	20050407	AU 2004-275696		20040722
CA 2533873	A1	20050407	CA 2004-2533873		20040722
EP 1651242	A2	20060503	EP 2004-809506		20040722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
JP 2007500697	T	20070118	JP 2006-521912		20040722
US 2007244059	A1	20071018	US 2006-565591		20061006 <--
PRIORITY APPLN. INFO.:			US 2003-490029P	P	20030728
			WO 2004-US23498	W	20040722

AB The present invention relates to the use of the cyclic dinucleotide c-di-GMP and cyclic dinucleotide analogs thereof in a method for attenuating virulence of a microbial pathogen or for inhibiting or reducing colonization by a microbial pathogen. This method further inhibits microbial biofilm formation and is capable of treating bacterial infections. The microbial colonization or biofilm formation inhibited or reduced may be on the skin or on nasal or mucosal surface. The microbial colonization or biofilm formation inhibited can also be on the surfaces of medical devices, especially those in close contact with the patient, as well on the surfaces of industrial and construction material where microbial colonization and biofilm formation is of concern.

IC ICM A61K031-00

CC 1-5 (Pharmacology)

ST attenuating virulence microbial pathogen inhibition biofilm GMP cyclic dinucleotide

IT Enterotoxins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(1, c-di-GMP downregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PBP-2, c-di-GMP upregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PBP-4, c-di-GMP upregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(RocS, for switching to rugose phenotype; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(VpsR, for switching to rugose phenotype; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agrA, c-di-GMP upregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agrB, c-di-GMP upregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using

c-di-GMP and cyclic dinucleotide analogs)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agrC, c-di-GMP upregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agrD, c-di-GMP upregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Antibacterial agents
Antibiotics
Biofilms (microbial)
Human
Mastitis
Mucous membrane
Pathogen
Salmonella enteritidis
Skin
Staphylococcus aureus
Vibrio cholerae
Virulence (microbial)
(attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Infection
(bacterial; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Enterotoxin A
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(c-di-GMP downregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Drug delivery systems
(carriers; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(clfA, c-di-GMP downregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(clfB, c-di-GMP downregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(collagen adhesin, c-di-GMP downregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Toxins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cytotoxins, vacuolating, c-di-GMP downregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic

dinucleotide analogs)
IT Oligonucleotides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dinucleotides, cyclic, analog; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Toxins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(exfoliative, c-di-GMP downregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fnbA, c-di-GMP downregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fnbB, c-di-GMP downregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(icaR, c-di-GMP downregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Drug delivery systems
(implants; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Mammary gland
(infection of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Nose
(mucosa; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(rsbW, c-di-GMP upregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(saeR, c-di-GMP upregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(saeS, c-di-GMP upregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)
IT Toxins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(toxic shock syndrome, c-di-GMP downregulating expression of; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)

IT 9012-56-0, Amidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(AmidB, for switching to rugose phenotype; attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)

IT 3353-33-1 60307-63-3 61093-23-0D, carboxy/phosphoalkylene ether derivs. 132182-18-4 132182-19-5 132182-21-9 132209-26-8 132294-58-7 232933-52-7 849214-01-3 849214-02-4 849214-03-5 849214-04-6 849214-05-7 849214-06-8 849214-07-9 849214-08-0 849214-09-1 849214-10-4 849214-11-5 849214-12-6 849214-13-7 849214-14-8 849214-15-9 849214-16-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)

IT 849447-99-0 849448-01-7 849448-02-8
RL: PRP (Properties)
(unclaimed nucleotide sequence; method for attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)

IT 849448-00-6 849448-03-9
RL: PRP (Properties)
(unclaimed protein sequence; method for attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)

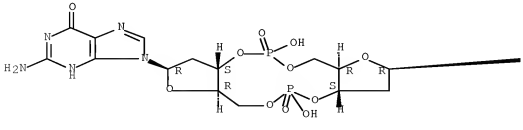
IT 60307-63-3 61093-23-0D, carboxy/phosphoalkylene ether derivs. 132182-18-4 132182-19-5 132182-21-9 132209-26-8 132294-58-7 232933-52-7 849214-01-3 849214-02-4 849214-03-5 849214-04-6 849214-05-7 849214-06-8 849214-07-9 849214-08-0 849214-09-1 849214-10-4 849214-11-5 849214-13-7 849214-15-9 849214-16-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuating virulence of microbial pathogens and inhibiting microbial biofilm formation by using c-di-GMP and cyclic dinucleotide analogs)

RN 60307-63-3 CAPLUS

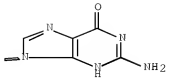
CN 3'-Guanylic acid, 2'-deoxyguanylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



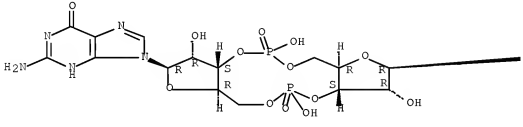
PAGE 1-B



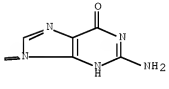
RN 61093-23-0 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



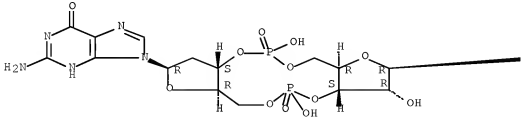
PAGE 1-B



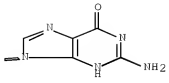
RN 132182-18-4 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

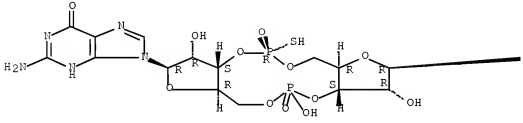


RN 132182-19-5 CAPLUS

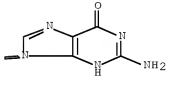
CN 3'-Guanylic acid, [P(R)]-P-thioguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



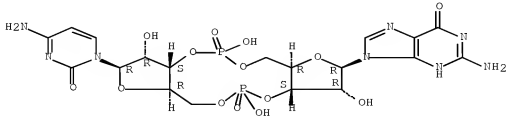
PAGE 1-B



RN 132182-21-9 CAPLUS

CN 3'-Guanylic acid, cytidylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

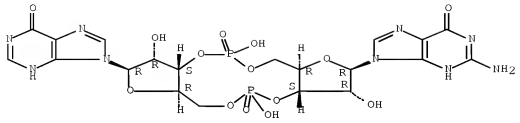
Absolute stereochemistry.



RN 132209-26-8 CAPLUS

CN 3'-Guanylic acid, inosinylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

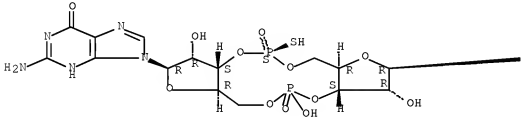


RN 132294-58-7 CAPLUS

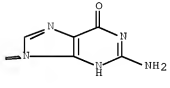
CN 3'-Guanylic acid, [P(S)]-P-thioguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



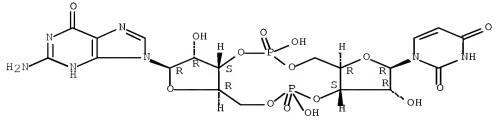
PAGE 1-B



RN 232933-52-7 CAPLUS

CN 3'-Guanylic acid, uridylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

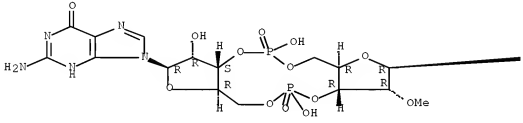


RN 849214-01-3 CAPLUS

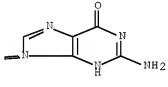
CN 3'-Guanylic acid, guanylyl-(3'→5')-2'-O-methyl-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

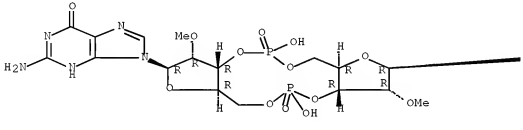


RN 849214-02-4 CAPLUS

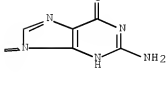
CN 3'-Guanylic acid, 2'-O-methylguanylyl-(3'→5')-2'-O-methyl-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

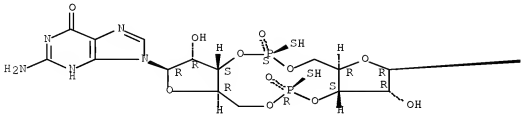


RN 849214-03-5 CAPLUS

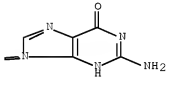
CN Guanosine, [P(R)]-P-thioguanylyl-(3'→5')-, 3'-[dihydrogen [P(S)]-phosphorothioate], cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



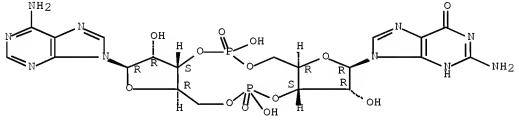
PAGE 1-B



RN 849214-04-6 CAPLUS

CN 3'-Guanylic acid, adenylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

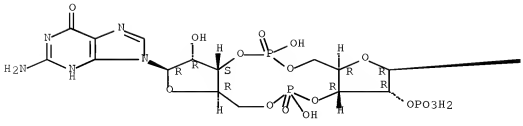


RN 849214-05-7 CAPLUS

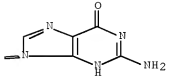
CN 2'-Guanylic acid, 5'-O-phosphonoguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

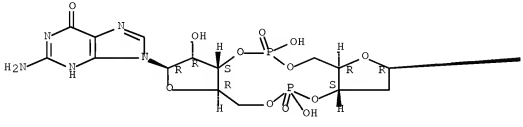


RN 849214-06-8 CAPLUS

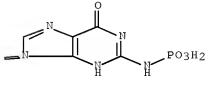
CN 3'-Guanylic acid, guanylyl-(3'→5')-N-phosphono-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

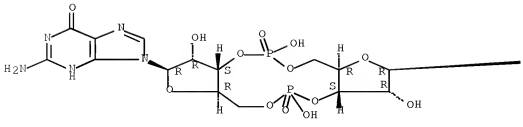


RN 849214-07-9 CAPLUS

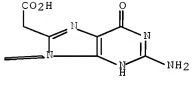
CN 3'-Guanylic acid, guanylyl-(3'→5')-8-(carboxymethyl)-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

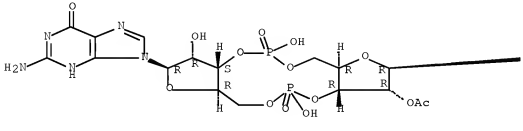


RN 849214-08-0 CAPLUS

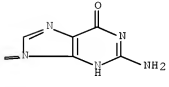
CN 3'-Guanylic acid, 2'-O-acetylguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

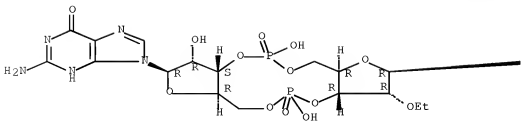


RN 849214-09-1 CAPLUS

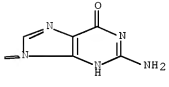
CN 3'-Guanylic acid, guanylyl-(3'→5')-2'-O-ethyl-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

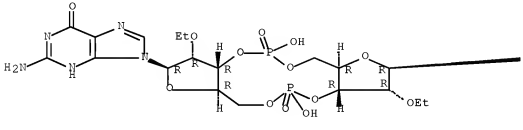


RN 849214-10-4 CAPLUS

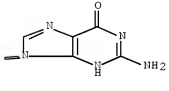
CN 3'-Guanylic acid, 2'-O-ethylguanylyl-(3'→5')-2'-O-ethyl-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

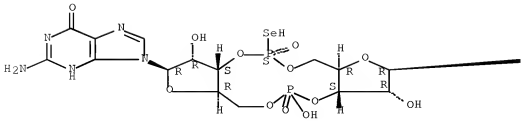


RN 849214-11-5 CAPLUS

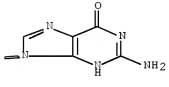
CN 3'-Guanylic acid, [P(S)]-P-selenoguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

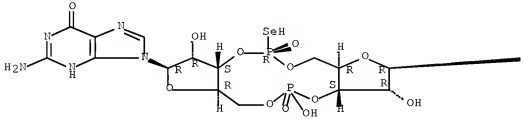


RN 849214-13-7 CAPLUS

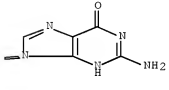
CN 3'-Guanylic acid, [P(R)]-P-selenoguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

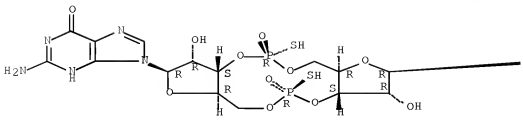


RN 849214-15-9 CAPLUS

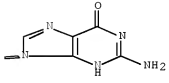
CN Guanosine, [P(R)]-P-thioguanylyl-(3'→5')-, 3'-[dihydrogen [P(R)]-phosphorothioate], cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

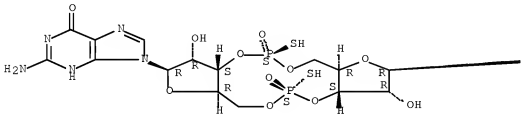


RN 849214-16-0 CAPLUS

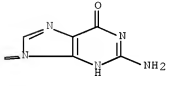
CN Guanosine, [P(S)]-P-thioguanylyl-(3'→5')-, 3'-[dihydrogen [P(S)]-phosphorothioate], cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L90 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2005:1005971 CAPLUS Full-text

DOCUMENT NUMBER: 143:279369

TITLE: Method using cyclic di-GMP or cyclic dinucleotide analog thereof for inhibiting cancer cell proliferation or increasing cancer cell apoptosis

INVENTOR(S): Karaolis, David K. R.; Raufman, Jean-Pierre
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005203051	A1	20050915	US 2005-79779	20050315
AU 2005221717	A1	20050922	AU 2005-221717	20050315
CA 2559802	A1	20050922	CA 2005-2559802	20050315
WO 2005087238	A2	20050922	WO 2005-US8447	20050315
WO 2005087238	A3	20060309		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005222626	A1	20050929	AU 2005-222626	20050315
CA 2560058	A1	20050929	CA 2005-2560058	20050315
WO 2005089777	A1	20050929	WO 2005-US8448	20050315
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1729781	A1	20061213	EP 2005-727318	20050315
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
EP 1740192	A2	20070110	EP 2005-753223	20050315
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007529531	T	20071025	JP 2007-503996	20050315
JP 2007529532	T	20071025	JP 2007-503997	20050315

PRIORITY APPLN. INFO.:
US 2004-552721P P 20040315
US 2004-563692P P 20040420
WO 2005-US8447 W 20050315
WO 2005-US8448 W 20050315

AB Cyclic di-GMP or cyclic dinucleotide analogs thereof can be used to inhibit cancer cell proliferation or to increase cancer cell apoptosis in vitro as well as in vivo in a patient.

IC ICM A61K031-7076
INCL 514045000
CC 1-6 (Pharmacology)
ST antitumor cyclic diGMP cancer cell proliferation apoptosis; cyclic

dinucleotide antitumor cancer cell proliferation apoptosis
IT Intestine, neoplasm
(colon; di-GMP or cyclic dinucleotide analog for inhibiting cancer cell proliferation or increasing cancer cell apoptosis)
IT Antitumor agents
Apoptosis
Brain, neoplasm
Drug delivery systems
Human
Leukemia
Lung, neoplasm
Lymphoma
Mammary gland, neoplasm
Neoplasm
Pancreas, neoplasm
Prostate gland, neoplasm
(di-GMP or cyclic dinucleotide analog for inhibiting cancer cell proliferation or increasing cancer cell apoptosis)
IT Oligonucleotides
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dinucleotides; di-GMP or cyclic dinucleotide analog for inhibiting cancer cell proliferation or increasing cancer cell apoptosis)
IT Nerve, neoplasm
(neuroblastoma; di-GMP or cyclic dinucleotide analog for inhibiting cancer cell proliferation or increasing cancer cell apoptosis)
IT Carcinoma
(squamous cell; di-GMP or cyclic dinucleotide analog for inhibiting cancer cell proliferation or increasing cancer cell apoptosis)
IT 85-32-5, 5'-GMP 7665-99-8, Cyclic GMP
RL: PAC (Pharmacological activity); BIOL (Biological study)
(di-GMP or cyclic dinucleotide analog for inhibiting cancer cell proliferation or increasing cancer cell apoptosis)
IT 60307-63-3 61093-23-0D, analogs 132182-18-4
132182-19-5 132182-21-9 132209-26-8
132294-58-7 232933-52-7 849214-03-5
849214-04-6 849214-05-7 849214-06-8
849214-07-9 849214-11-5 849214-13-7
849214-15-9 864357-81-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(di-GMP or cyclic dinucleotide analog for inhibiting cancer cell proliferation or increasing cancer cell apoptosis)
IT 60307-63-3 61093-23-0D, analogs 132182-18-4
132182-19-5 132182-21-9 132209-26-8
132294-58-7 232933-52-7 849214-03-5
849214-04-6 849214-05-7 849214-06-8
849214-07-9 849214-11-5 849214-13-7
849214-15-9 864357-81-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(di-GMP or cyclic dinucleotide analog for inhibiting cancer cell proliferation or increasing cancer cell

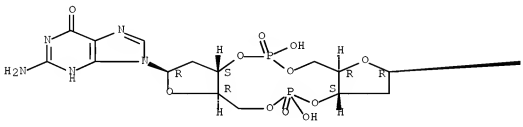
apoptosis)

RN 60307-63-3 CAPLUS

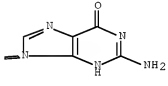
CN 3'-Guanylic acid, 2'-deoxyguanylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

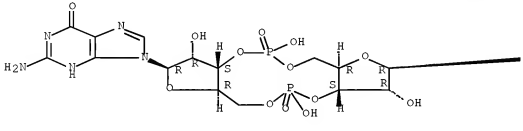


RN 61093-23-0 CAPLUS

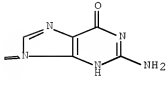
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

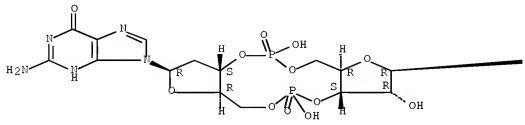


RN 132182-18-4 CAPLUS

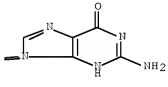
CN 3'-Guanylic acid, guanylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

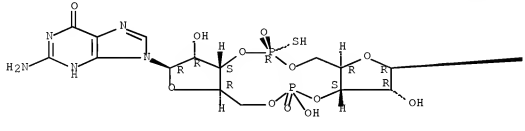


RN 132182-19-5 CAPLUS

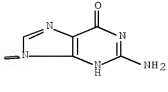
CN 3'-Guanylic acid, [P(R)]-P-thioguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

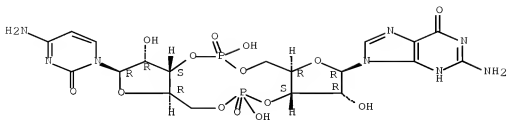


RN 132182-21-9 CAPLUS

CN 3'-Guanylic acid, cytidylyl-(3'→5')-, cyclic nucleotide (9CI) (CA

INDEX NAME)

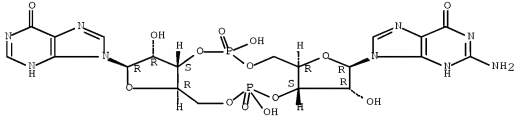
Absolute stereochemistry.



RN 132209-26-8 CAPLUS

CN 3'-Guanylic acid, inosinylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

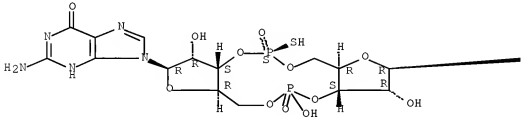


RN 132294-58-7 CAPLUS

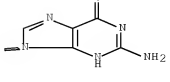
CN 3'-Guanylic acid, [P(S)]-P-thioguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

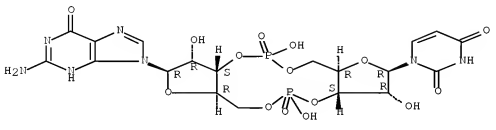


PAGE 1-B



RN 232933-52-7 CAPLUS
CN 3'-Guanylic acid, uridylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

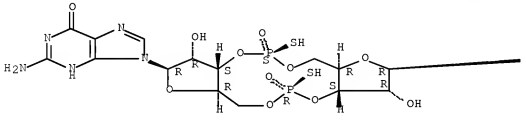
Absolute stereochemistry. Rotation (-).



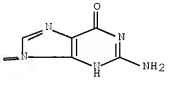
RN 849214-03-5 CAPLUS
CN Guanosine, [P(R)]-P-thioguanylyl-(3'→5')-, 3'-[dihydrogen [P(S)]-phosphorothioate], cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

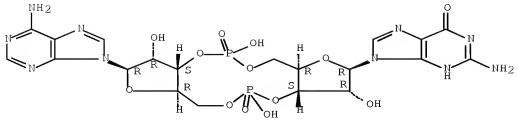


PAGE 1-B



RN 849214-04-6 CAPLUS
CN 3'-Guanylic acid, adenylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

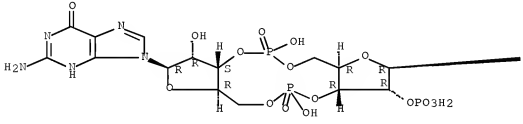
Absolute stereochemistry.



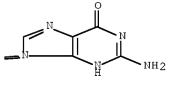
RN 849214-05-7 CAPLUS
CN 2'-Guanylic acid, 5'-O-phosphonoguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



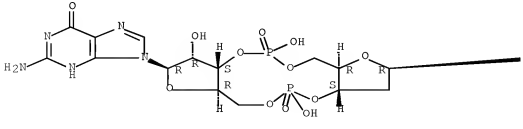
PAGE 1-B



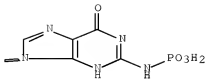
RN 849214-06-8 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-N-phosphono-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



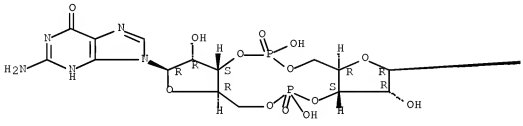
PAGE 1-B



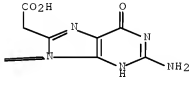
RN 849214-07-9 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-8-(carboxymethyl)-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



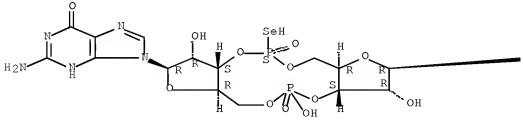
PAGE 1-B



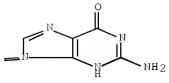
RN 849214-11-5 CAPLUS
CN 3'-Guanylic acid, [P(S)]-P-selenoguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

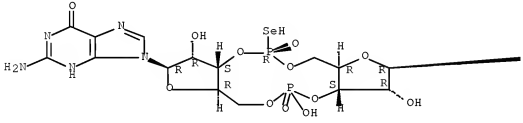


RN 849214-13-7 CAPLUS

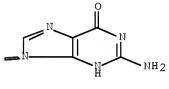
CN 3'-Guanylic acid, [P(R)]-P-selenoguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

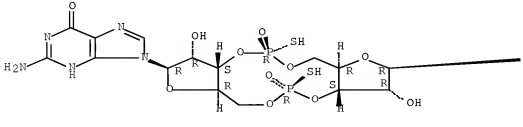


RN 849214-15-9 CAPLUS

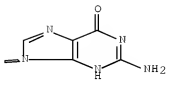
CN Guanosine, [P(R)]-P-thioguanylyl-(3'→5')-, 3'-[dihydrogen [P(R)]-phosphorothioate], cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



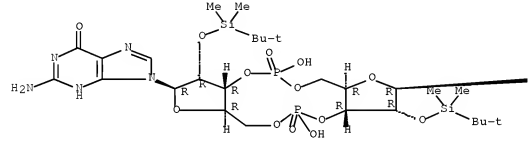
PAGE 1-B



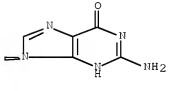
RN 864357-81-3 CAPLUS
CN 3'-Guanylic acid, 2'-O-[(1,1-dimethylethyl)dimethylsilyl]guanylyl-(3'→5')-2'-O-[(1,1-dimethylethyl)dimethylsilyl]-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L90 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 5

ACCESSION NUMBER:	2005:714247 CAPLUS Full-text
DOCUMENT NUMBER:	143:205833
TITLE:	3',5'-Cyclic diguanylic acid reduces the virulence of biofilm-forming Staphylococcus aureus strains in a mouse model of mastitis infection
AUTHOR(S):	Brouillette, Eric; Hyodo, Mamoru; Hayakawa, Yoshihiro; Karaolis, David K. R.; Malouin, Francois
CORPORATE SOURCE:	Centre d'Etude et de Valorisation de la Diversite Microbienne (CEVDM), Departement de biologie, Faculte des sciences, Universite de Sherbrooke, Sherbrooke, QC, J1K 2R1, Can.
SOURCE:	Antimicrobial Agents and Chemotherapy (2005), 49(8), 3109-3113

CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The cyclic dinucleotide 3',5'-cyclic diguanylic acid (c-di-GMP) is a naturally occurring small mol. that regulates important signaling systems in bacteria. The authors have recently shown that c-di-GMP inhibits Staphylococcus aureus biofilm formation in vitro and its adherence to HeLa cells. The authors now report that c-di-GMP treatment has an antimicrobial and antipathogenic activity in vivo and reduces, in a dose-dependent manner, bacterial colonization by biofilm-forming S. aureus strains in a mouse model of mastitis infection. Intramammary injections of 5 and 50 nmol of c-di-GMP decreased colonization (bacterial CFU) per g of gland by 0.79 ($P > 0.05$) and 1.44 ($P < 0.01$) logs, resp., whereas 200-nmol doses allowed clearance of the bacteria below the detection limit with a reduction of more than 4 logs ($P < 0.001$) compared to the untreated control groups. These results indicate that cyclic dinucleotides potentially represent an attractive and novel drug platform which could be used alone or in combination with other agents or drugs in the prevention, treatment, or control of infection.

CC 1-5 (Pharmacology)

IT 61093-23-0, 3',5'-Cyclic diguanylic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3',5'-cyclic diguanylic acid reduces the virulence of biofilm-forming Staphylococcus aureus strains in a mouse model of mastitis infection)

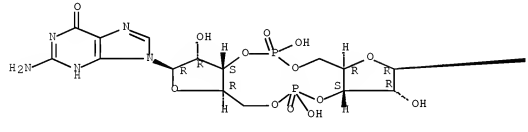
IT 61093-23-0, 3',5'-Cyclic diguanylic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3',5'-cyclic diguanylic acid reduces the virulence of biofilm-forming Staphylococcus aureus strains in a mouse model of mastitis infection)

RN 61093-23-0 CAPLUS

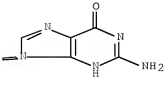
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS

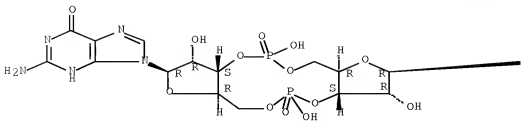
L90 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2005:229578 CAPLUS Full-text
DOCUMENT NUMBER: 142:426617
TITLE: c-di-GMP (3'-5'-cyclic diguanylic acid) inhibits Staphylococcus aureus cell-cell interactions and biofilm formation
AUTHOR(S): Karaolis, David K. R.; Rashid, Mohammed H.; Chythanya, Rajanna; Luo, Wensheng; Hyodo, Mamoru; Hayakawa, Yoshihiro
CORPORATE SOURCE: Department of Epidemiology and Preventive Medicine, University of Maryland School of Medicine, Baltimore, MD, 21201, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2005), 49(3), 1029-1038
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Staphylococcus aureus is an important pathogen of humans and animals, and antibiotic resistance is a public health concern. Biofilm formation is essential in virulence and pathogenesis, and the ability to resist antibiotic treatment results in difficult-to-treat and persistent infections. As such, novel antimicrobial approaches are of great interest to the scientific, medical, and agriculture communities. We recently proposed that modulating levels of the cyclic dinucleotide signaling mol., c-di-GMP (cyclic diguanylate [3',5'-cyclic diguanylic acid], cGpGp), has utility in regulating phenotypes of prokaryotes. We report that extracellular c-di-GMP shows activity against human clin. and bovine intramammary mastitis isolates of S. aureus, including methicillin-resistant S. aureus (MRSA) isolates. We show that chemical synthesized c-di-GMP is soluble and stable in water and physiol. saline and stable following boiling and exposure to acid and alkali. Treatment of S. aureus with extracellular c-di-GMP inhibited cell-to-cell (intercellular) adhesive interactions in liquid medium and reduced (>50%) biofilm formation in human and bovine isolates compared to untreated controls. C-di-GMP inhibited the adherence of S. aureus to human epithelial HeLa cells. The cyclic nucleotide analogs cGMP and cAMP had a lesser inhibitory effect on biofilms, while 5'-GMP had no major effect. We propose that cyclic dinucleotides such as c-di-GMP, used either alone or in combination with other antimicrobial agents, represent a novel and attractive approach in the development of intervention strategies for the prevention of biofilms and the control and treatment of infection.

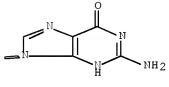
CC 10-3 (Microbial, Algal, and Fungal Biochemistry)
IT 61093-23-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(c-di-GMP (3'-5'-cyclic diguanylic acid) inhibits Staphylococcus aureus cell-cell interactions and biofilm formation)
IT 61093-23-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(c-di-GMP (3'-5'-cyclic diguanylic acid) inhibits Staphylococcus aureus cell-cell interactions and biofilm formation)
RN 61093-23-0 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L90 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 7

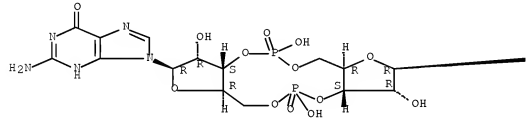
ACCESSION NUMBER: 2005:150086 CAPLUS Full-text
DOCUMENT NUMBER: 142:329238
TITLE: 3',5'-Cyclic diguanylic acid (c-di-GMP) inhibits basal and growth factor-stimulated human colon cancer cell proliferation
AUTHOR(S): Karaolis, David K. R.; Cheng, Kunrong; Lipsky, Michael; Elnabawi, Ahmed; Catalano, Jennifer; Hyodo, Mamoru; Hayakawa, Yoshihiro; Raufman, Jean-Pierre
CORPORATE SOURCE: Department of Epidemiology and Preventive Medicine, University of Maryland School of Medicine, Baltimore, MD, 21201, USA
SOURCE: Biochemical and Biophysical Research Communications (2005), 329(1), 40-45
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The novel cyclic dinucleotide, 3',5'-cyclic diguanylic acid, cGpGp (c-di-GMP), is a naturally occurring small mol. that regulates important signaling mechanisms in prokaryotes. Recently, we showed that c-di-GMP has "drug-like" properties and that c-di-GMP treatment might be a useful antimicrobial approach to attenuate the virulence and pathogenesis of Staphylococcus aureus and prevent or treat infection. In the present communication, we report that c-di-GMP (≥50 μM) has striking properties regarding inhibition of cancer cell proliferation in vitro. c-di-GMP inhibits both basal and growth factor (acetylcholine and epidermal growth factor)-induced cell proliferation of human colon cancer (H508) cells. Toxicity studies revealed that exposure of normal rat kidney cells and human neuroblastoma cells to c-di-GMP at biol. relevant doses showed no lethal cytotoxicity. Cyclic dinucleotides, such as c-di-GMP, represent an attractive and novel "drug-platform technol." that can be used not only to develop new antimicrobial agents, but also to develop novel therapeutic agents to prevent or treat cancer.

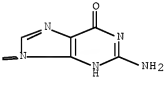
CC 1-6 (Pharmacology)
IT 61093-23-0
RL: PAC (Pharmacological activity); BIOL (Biological study)
(3',5'-Cyclic diguanylic acid inhibits basal and growth factor-stimulated human colon cancer cell proliferation)
IT 61093-23-0
RL: PAC (Pharmacological activity); BIOL (Biological study)
(3',5'-Cyclic diguanylic acid inhibits basal and growth factor-stimulated human colon cancer cell proliferation)
RN 61093-23-0 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L90 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1396598 CAPLUS Full-text
DOCUMENT NUMBER: 148:24432
TITLE: Method for stimulating the immune, inflammatory or neuroprotective response
INVENTOR(S): Karaolis, David K. R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 60pp., Cont.-in-part of U.S. Ser. No. 79,886.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2007281897	A1	20071206	US 2007-669006	20070130
AU 2005221717	A1	20050922	AU 2005-221717	20050315

CA 2559802	A1	20050922	CA 2005-2559802		20050315
AU 2005222626	A1	20050929	AU 2005-222626		20050315
CA 2560058	A1	20050929	CA 2005-2560058		20050315
US 2006040887	A1	20060223	US 2005-79886		20050315
EP 1729781	A1	20061213	EP 2005-727318		20050315
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR					
EP 1740192	A2	20070110	EP 2005-753223		20050315
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR					
JP 2007529531	T	20071025	JP 2007-503996		20050315
JP 2007529532	T	20071025	JP 2007-503997		20050315
PRIORITY APPLN. INFO.:			US 2004-552721P	P	20040315
			US 2004-563692P	P	20040420
			US 2005-79886	A2	20050315
			WO 2005-US8447	W	20050315
			WO 2005-US8448	W	20050315

AB Cyclic di-GMP, or a cyclic dinucleotide analog thereof that has the same effect as cyclic di-GMP, stimulates or enhances immune or inflammatory response in a patient or enhances the immune response to a vaccine by serving as an adjuvant. Cyclic di-GMP, or a cyclic dinucleotide analog thereof, also has neuroprotective properties for use as a neuroprotective agent to inhibit, treat, or ameliorate the effects of injuries, diseases,.

INCL 514044000

CC 1-7 (Pharmacology)
Section cross-reference(s): 15

ST cyclic dinucleotide analog immunostimulant
neuroprotective inflammation stimulation; diGMP cyclic immunostimulant
neuroprotective inflammation stimulation

IT 60307-63-3 132182-18-4 132182-21-9
132209-26-8 132294-58-7 232933-52-7D, derivs.
849214-04-6 849214-05-7 849214-06-8
849214-11-5 849214-13-7 849214-15-9
864357-81-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for stimulating the immune, inflammatory or neuroprotective response in relation to treatment of infections or enhancement of vaccination)

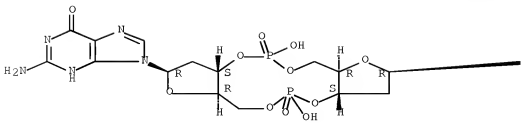
IT 60307-63-3 132182-18-4 132182-21-9
132209-26-8 132294-58-7 232933-52-7D, derivs.
849214-04-6 849214-05-7 849214-06-8
849214-11-5 849214-13-7 849214-15-9
864357-81-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for stimulating the immune, inflammatory or neuroprotective response in relation to treatment of infections or enhancement of vaccination)

RN 60307-63-3 CAPLUS

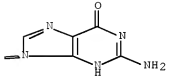
CN 3'-Guanylic acid, 2'-deoxyguanylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

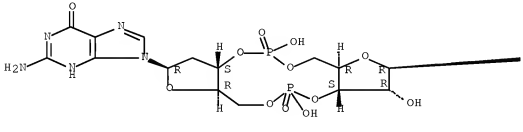


RN 132182-18-4 CAPLUS

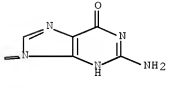
CN 3'-Guanylic acid, guanylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



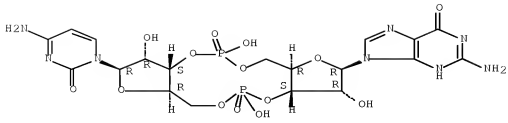
PAGE 1-B



RN 132182-21-9 CAPLUS

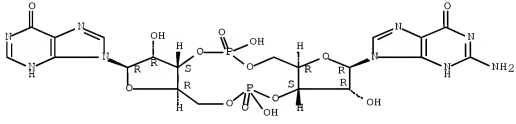
CN 3'-Guanylic acid, cytidylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 132209-26-8 CAPLUS
CN 3'-Guanylic acid, inosinylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

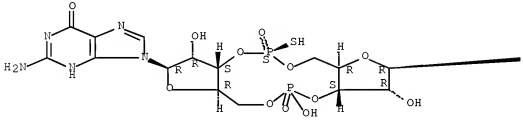
Absolute stereochemistry.



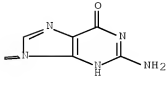
RN 132294-58-7 CAPLUS
CN 3'-Guanylic acid, [P(S)]-P-thioguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



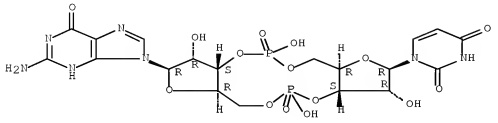
PAGE 1-B



RN 232933-52-7 CAPLUS

CN 3'-Guanylic acid, uridylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

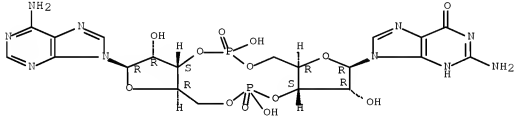
Absolute stereochemistry. Rotation (-).



RN 849214-04-6 CAPLUS

CN 3'-Guanylic acid, adenylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

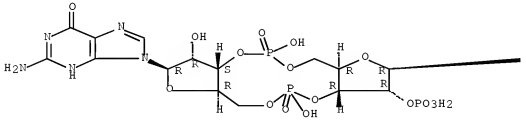


RN 849214-05-7 CAPLUS

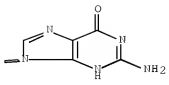
CN 2'-Guanylic acid, 5'-O-phosphonoguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



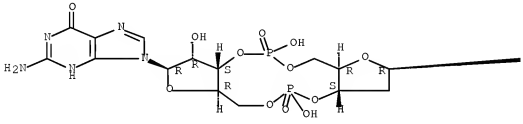
PAGE 1-B



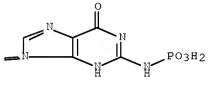
RN 849214-06-8 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-N-phosphono-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



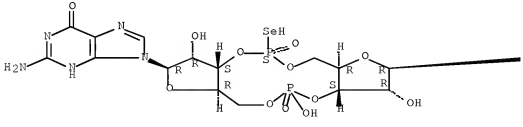
PAGE 1-B



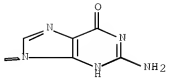
RN 849214-11-5 CAPLUS
CN 3'-Guanylic acid, [P(S)]-P-selenoguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

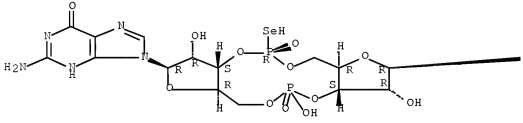


RN 849214-13-7 CAPLUS

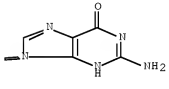
CN 3'-Guanylic acid, [P(R)]-P-selenoguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

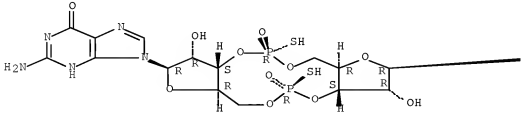


RN 849214-15-9 CAPLUS

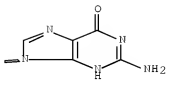
CN Guanosine, [P(R)]-P-thioguanylyl-(3'→5')-, 3'-[dihydrogen [P(R)]-phosphorothioate], cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



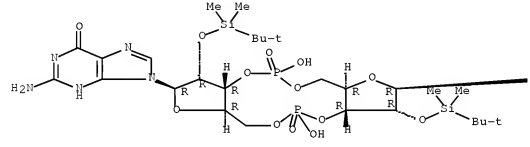
PAGE 1-B



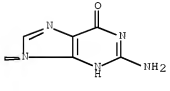
RN 864357-81-3 CAPLUS
CN 3'-Guanylic acid, 2'-O-[(1,1-dimethylethyl)dimethylsilyl]guanylyl-(3'→5')-2'-O-[(1,1-dimethylethyl)dimethylsilyl]-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L90 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:351606 CAPLUS Full-text
DOCUMENT NUMBER: 145:189078
TITLE: Organic synthesis, chemical properties, and biological activities of cyclic bis(3'-5)diguanylic acid (c-di-GMP) and its analogs
AUTHOR(S): Hyodo, Mamoru; Hayakawa, Yoshihiro; Karaolis, David K. R.
CORPORATE SOURCE: Graduate School of Human Informatics/Information Science, CREST/JST, Nagoya University, Chikusa, Nagoya, 464-8601, Japan
SOURCE: Yuki Gosei Kagaku Kyokaishi (2006), 64(4), 359-370
CODEN: YGKKAE; ISSN: 0037-9980
PUBLISHER: Yuki Gosei Kagaku Kyokai

DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review. This paper describes efficient synthesis, chemical behaviors, and biol. activities of cyclic bis(3'-5')diguanylic acid (c-di-GMP) and its analogs, including cyclic bis(3'-5')guanylic-inosinic acid (c-GpIp), cyclic bis(3'-5')guanylic-adenylic acid (c-GpAp), and bis(3'-5')diguanylic acid monophosphorothioate (c-GpGps). C-di-GMP was synthesized via two methods. Between the two methods, one method is more effective, particularly, for large-scale (gram-scale) synthesis to obtain the target compound in a high yield. While, c-GpIp, c-GpAp, and c-GpGps were synthesized via similar strategies. Studies on chemical behaviors of c-di-GMP indicated that these cyclic dinucleotides exist as the monomers in aprotic solvents such as DMSO. By contrast, it was shown that c-di-GMP smoothly aggregates to form a mixture of many compds. in water, in < 0.9% sodium chloride solns., in < 100 mM phosphate buffer solns., and in < 100 mM ammonium acetate buffer solns. All aggregated compds. smoothly revert to a single compound (probably an aggregate) by dissolving in a 0.9% sodium chloride solution (a physiol. salt solution), a > 100 mM phosphate buffer solution, or a > 100 mM ammonium acetate buffer solution Biol. investigation disclosed some novel activities of c-di-GMP, such as inhibition of biofilm formation of Staphylococcus aureus, inhibition of basal and growth factor stimulated human colon cancer cell proliferation, and reduction of the villus of biofilm-formed Staphylococcus aureus in a mouse model.

CC 33-0 (Carbohydrates)
Section cross-reference(s): 1

IT 61093-23-0P 132209-26-8P 849214-04-6P
885464-60-8P
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, chemical properties, and biol. activities of cyclic bis(3'-5)diguanylic acid (c-di-GMP) and its analogs)

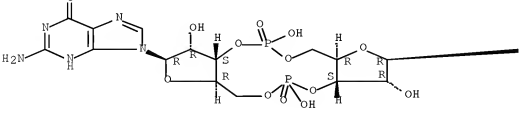
IT 61093-23-0P 132209-26-8P 849214-04-6P
885464-60-8P
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, chemical properties, and biol. activities of cyclic bis(3'-5)diguanylic acid (c-di-GMP) and its analogs)

RN 61093-23-0 CAPLUS

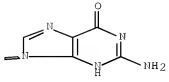
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

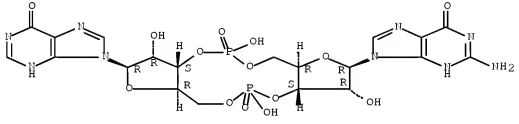


PAGE 1-B



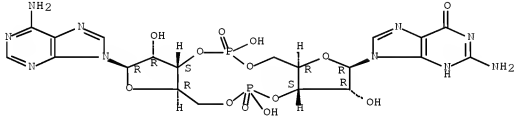
RN 132209-26-8 CAPLUS
CN 3'-Guanylic acid, inosinylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 849214-04-6 CAPLUS
CN 3'-Guanylic acid, adenylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

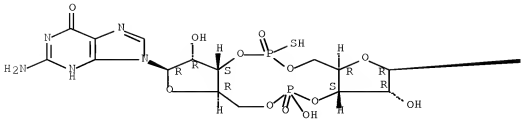
Absolute stereochemistry.



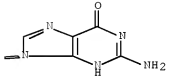
RN 885464-60-8 CAPLUS
CN 3'-Guanylic acid, P-thioguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L90 ANSWER 10 OF 12 MEDLINE on STN DUPLICATE 8

ACCESSION NUMBER:	2003491220 MEDLINE Full-text
DOCUMENT NUMBER:	PubMed ID: 14568156
TITLE:	Identification of genes involved in the switch between the smooth and rugose phenotypes of Vibrio cholerae.
AUTHOR:	Rashid Mohammed H; Rajanna Chythanya; Ali Afsar; Karaolis David K R
CORPORATE SOURCE:	Department of Epidemiology and Preventive Medicine, University of Maryland School of Medicine, Baltimore, MD 21201, USA.. karaolis@umaryland.edu
CONTRACT NUMBER:	AI45637 (United States NIAID)
SOURCE:	FEMS microbiology letters, (2003 Oct 10) Vol. 227, No. 1, pp. 113-9. Journal code: 7705721. ISSN: 0378-1097.
PUB. COUNTRY:	Netherlands
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	200402
ENTRY DATE:	Entered STN: 22 Oct 2003 Last Updated on STN: 24 Feb 2004 Entered Medline: 23 Feb 2004

ABSTRACT:

Vibrio cholerae can switch to a 'rugose' phenotype characterized by an exopolysaccharide (EPS) matrix, wrinkled colony morphology, increased biofilm formation and increased survival under specific conditions. The vps gene cluster responsible for the biosynthesis of the rugose EPS (rEPS) is positively regulated by VpsR. We recently identified media (APW#3) promoting EPS production and the rugose phenotype and found epidemic strains switch at a higher frequency than non-pathogenic strains, suggesting this switch and the rugose phenotype are important in cholera

epidemiology. In this study, transposon mutagenesis on a smooth V. cholerae strain was used to identify mutants that were unable to shift to the rugose phenotype under inducing conditions to better understand the molecular basis of the switch. We identified vpsR, galE and vps previously associated with the rugose phenotype, and also identified genes not previously associated with the phenotype, including rfbD and rfbE having roles in LPS (lipopolysaccharide) synthesis and aroB and aroK with roles in aromatic amino acid synthesis. Additionally, a mutation in amiB encoding N-acetylmuramoyl-L-alanine amidase caused defects in the switch, motility and cell morphology. We also found that a gene encoding a novel regulatory protein we termed RocS (regulation of cell signaling) containing a GGDEF and EAL domains and associated with c-di-GMP levels is important for the rugose phenotype, EPS, biofilm formation and motility. We propose that modulation of cyclic ***dinucleotide*** (e.g. c-di-GMP) levels might have application in regulating various phenotypes of prokaryotes. Our study shows the molecular complexity of the switch between the smooth and rugose phenotypes of V. cholerae and may be relevant to similar phenotypes in other species.

CONTROLLED TERM: *Biofilms
DNA Transposable Elements
Genes, Bacterial: GE, genetics
*Genes, Bacterial: PH, physiology
Mutagenesis, Insertional
Phenotype
*Polysaccharides, Bacterial: ME, metabolism
Polysaccharides, Bacterial: PH, physiology
Vibrio cholerae: CL, classification
Vibrio cholerae: GE, genetics
*Vibrio cholerae: PH, physiology

CHEMICAL NAME: 0 (DNA Transposable Elements); 0 (Polysaccharides, Bacterial)

L90 ANSWER 11 OF 12 MEDLINE on STN

ACCESSION NUMBER: 2006714149 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17150661
TITLE: Chemical behavior of bis(3'-5')diguanylic acid in aqueous solutions.
AUTHOR: Hyodo Mamoru; Sato Yumi; Hayakawa Yoshihiro; Karaolis David K R
CORPORATE SOURCE: Graduate School of Information Science/Human Informatics, and CREST/JST, Nagoya University, Chikusa, Nagoya 464-8601, Japan.
SOURCE: Nucleic acids symposium series (2004), (2005) No. 49, pp. 117-8.
Journal code: 101259965. E-ISSN: 1746-8272.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200706
ENTRY DATE: Entered STN: 12 Dec 2006
Last Updated on STN: 13 Jun 2007
Entered Medline: 12 Jun 2007

ABSTRACT:
This paper describes unique behavior of bis(3'-5')diguanylic acid (c-di-GMP) under some conditions. Thus, c-di-GMP exists as the monomer in aprotic organic solvents such as DMSO. By contrast, c-di-GMP smoothly aggregates in water and in low-concentration aqueous solutions of some salts, such as sodium chloride and ammonium acetate, to give a mixture of many aggregates. The resulting multiple aggregates converge to the single compound (provably the monomer) in a

>154 mM (0.9%) sodium chloride aqueous solution, in a >100 mM ammonium acetate buffer, and in a >100 mM phosphate buffer.
CONTROLLED TERM: Buffers
Chromatography, High Pressure Liquid
*Cyclic GMP: AA, analogs & derivatives
Cyclic GMP: CH, chemistry
Magnetic Resonance Spectroscopy
Solutions
Solvents: CH, chemistry
Water: CH, chemistry
CAS REGISTRY NO.: 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7665-99-8 (Cyclic GMP); 7732-18-5 (Water)
CHEMICAL NAME: 0 (Buffers); 0 (Solutions); 0 (Solvents)

L90 ANSWER 12 OF 12 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-478020 [49] WPIX
CROSS REFERENCE: 2005-648062
DOC. NO. CPI: C2006-150844 [49]
TITLE: Modulating immune or inflammatory response in patient and therefore treating immunological or inflammatory diseases e.g. cancer, arthritis and infectious diseases, involves administering cyclic di-GMP or its cyclic dinucleotide analogue
DERWENT CLASS: B04; D16
INVENTOR: KARAOLIS D K R
PATENT ASSIGNEE: (KARA-I) KARAOLIS D K R
COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20060040887	A1	20060223	(200649)*	EN	28[5]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20060040887	A1 Provisional	US 2004-552721P	20040315
US 20060040887	A1 Provisional	US 2004-563692P	20040420
US 20060040887	A1	US 2005-79886	20050315

PRIORITY APPLN. INFO: US 2005-79886 20050315
US 2004-552721P 20040315
US 2004-563692P 20040420
INT. PATENT CLASSIF.:
IPC ORIGINAL: A61K0031-7042 [I,C]; A61K0031-7076 [I,A]
USCLASS NCLM: 514/045.000
BASIC ABSTRACT:
US 20060040887 A1 UPAB: 20060801
NOVELTY - Modulating (M1) immune or inflammatory response in a patient comprising administering an effective amount of cyclic di-GMP or its cyclic dinucleotide analogue to a patient in need of the modulation of immune or inflammatory response, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) stimulating or enhancing (M2) an immune response in a patient comprising activating dendritic cells or T cells with an antigen and with cyclic di-GMP or its cyclic dinucleotide analogue, and administering the activated dendritic cells or T cells as a cellular vaccine to stimulate or enhance an immune response in the patient;

(2) inhibiting, treating or ameliorating (M3) the effects of an injury, disease, disorder or condition that result in neuronal degeneration comprising administering to a patient in their need, an effective amount of cyclic di-GMP or its cyclic dinucleotide analogue to inhibit, treat, or ameliorate the effects of the injury, disease, disorder or condition that result in neuronal degeneration in the patient; and (3) an immunizing composition comprising a vaccine or antigen and cyclic di-GMP or its cyclic dinucleotide analogue.

ACTIVITY - Antiarthritic; Cytostatic; Immunosuppressive; Antimicrobial; Antiallergic; Antiasthmatic; Neuroprotective; Vulnerary; Tranquilizer; Cerebroprotective; Vasotropic; Ophthalmological; Nootropic; Antiparkinsonian.

MECHANISM OF ACTION - Stimulates and activates dendritic cells, T cell and Th-1 response; Up-regulates expression of costimulatory molecules and proinflammatory response. Neuroprotective effect of c-di-GMP was tested as follows.

Hippocampi were dissected from the brain of 18-day-old fetal rats. Following enzymatic and mechanical dissociation, cells were plated at a density of 100000 cells/well in 96-well plates pre-coated with matrigel. At the seventh day after plating, cultures were subjected to one of the following treatments vehicle (24 hours), STS (100 nM, 22 hours), c-di-GMP (24 hours, c-di-GMP (2 hours) followed by c-di-GMP-plus-STS (22 hours), c-di-GMP-plus-STS (24 hours), or STS (2 hours) followed by c-di-GMP-plus-STS (22 hours). At the end of the treatments, cell viability was analyzed. The assay involves the spectrophotometric measurement (at 490 nm) of the mitochondrial conversion of a tetrazolium dye into a colorful product. The absorbance of the assay correlates with the number of metabolically active cells. The results showed that hippocampal cells were sensitive to c-di-GMP. Pre-treatment of the cultures with c-d-GMP (0.1-10 microM) prevented the STS-induced cell death. When c-di-GMP (0.1-10 microM) was applied to the cultures together with or after STS, the number of metabolic active cells was on average higher than that observed in cultures treated with STS alone. The c-di-GMP had neuroprotective properties.

USE - (M1) is useful for modulating immune or inflammatory response in patient, preferably stimulating or enhancing an immune or inflammatory response in a patient. (M1) is useful for treating an immunological or inflammatory disorder or disease by stimulating or enhancing immune or inflammatory response in the patient. The immunological or inflammatory disorder is chosen from arthritis, cancer, autoimmune disorder or disease, allergic reaction, chronic infectious disease, infectious disease in which the pathogen or toxin produced impairs the immune response, and an immunodeficiency disease or disorder. (M1) is useful for inhibiting or treating an allergic reaction, where the allergic reaction is asthma. (M2) is useful for stimulating or enhancing an immune response in a patient. (M3) is useful for inhibiting, treating or ameliorating the effects of an injury, disease, disorder or condition that result in neuronal degeneration. The injury, disease, disorder or condition is chosen from spinal cord injury, blunt trauma, penetrating trauma, hemorrhagic stroke, and ischemic stroke. The injury, disease, disorder, or condition is neurodegenerative disease, disorder or condition. The neurodegenerative disease, disorder or condition is chosen from glaucoma, Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis (all claimed).

ADVANTAGE - (M1) enables to effectively stimulate or enhance the immune or inflammatory response in the patient. MANUAL CODE: CPI: B04-B03B; B04-

B03E; B04-B04C; B04-C02; B04-E01;
B04-F04; B04-N04; B14-A01; B14-A02; B14-C09; B14-F02D1;
B14-F08; B14-G01; B14-G02A; B14-G02D; B14-H01; B14-J01;
B14-N03A; B14-N16; B14-S11; D05-H07; D05-H08

ABEX ADMINISTRATION - Administration of the c-di-GMP or its cyclic dinucleotide analogue is by parenteral e.g. intravenous, intraperitoneal, intramuscular, subcutaneous, mucosal (e.g. oral, intranasal, buccal, vaginal, rectal, intraocular), intrathecal, topical, and intradermal routes, at a dosage ranging from 0.1-100 microM, more preferably 1-10 microM.

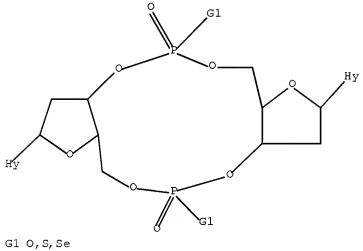
EXAMPLE - No suitable example given.

TECH

BIOTECHNOLOGY - Preferred Method: (M1) preferably involves stimulating or enhancing the immune or inflammatory response in the patient. (M1) involves administering an effective amount of cyclic di-GMP or its cyclic dinucleotide analogue to a patient in their need, to stimulate or enhance the immune or inflammatory response in the patient. The cyclic dinucleotide analogue is chosen from any one of 20 cyclic dinucleotide compounds e.g. compound of formula (I) and (XV). The immune response stimulated or enhanced includes a Th1 oriented immune response. (M1) enhances immune response to a vaccine, where an effective amount of a vaccine or antigen is administered to the patient in their need in combination with an effective amount of cyclic di-GMP or its cyclic dinucleotide analogue. The immune response is a cellular response. The vaccine is chosen from protein vaccine, polysaccharide vaccine, DNA vaccine, live attenuated vaccine, and a killed vaccine. The vaccine is a cancer vaccine. The cancer vaccine is an autologous or allogeneic cancer vaccine.

SEARCH OF BROAD STRUCTURE + TEXT

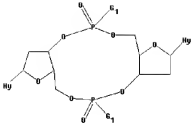
```
=> fil reg
FILE 'REGISTRY' ENTERED AT 15:36:56 ON 19 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   18 MAR 2008  HIGHEST RN 1008796-87-9
DICTIONARY FILE UPDATES:  18 MAR 2008  HIGHEST RN 1008796-87-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> d stat que l13
L8                STR
```

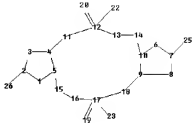


G1 O,S,Se

Structure attributes must be viewed using STN Express query preparation.

Uploading L8.str





```
chain nodes :
19  20  22  23  25  26
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  17  18
chain bonds :
2-26  7-25  12-20  12-22  17-19  17-23
ring bonds :
1-2  1-5  2-3  3-4  4-5  4-11  5-15  6-7  6-10  7-8  8-9  9-10  9-18  10-14  11-12
12-13  13-14  15-16  16-17  17-18
exact/norm bonds :
1-2  1-5  2-3  2-26  3-4  4-5  4-11  5-15  6-7  6-10  7-8  7-25  8-9  9-10  9-18
10-14  11-12  12-13  12-20  12-22  13-14  15-16  16-17  17-18  17-19  17-23


G1:O,S,Se

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:CLASS
20:CLASS  22:CLASS  23:CLASS  25:CLASS  26:Atom
Generic attributes :
25:
Saturation              : Unsaturated
26:
Saturation              : Unsaturated

Element Count :
Node 25: Limited
    N,N2

Node 26: Limited
    N,N2
```

```
L13         136 SEA FILE=REGISTRY SSS FUL L8

100.0% PROCESSED    1696 ITERATIONS                          136 ANSWERS
SEARCH TIME: 00.00.01


=> fil capl; d que nos 133; d que nos 135; d que nos 137; d que nos 141
FILE 'CAPLUS' ENTERED AT 15:37:21 ON 19 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 19 Mar 2008  VOL 148 ISS 12
FILE LAST UPDATED: 18 Mar 2008  (20080318/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE


L8              STR
L13         136 SEA FILE=REGISTRY SSS FUL L8
L14         149 SEA FILE=CAPLUS ABB=ON  L13
L17       33297 SEA FILE=CAPLUS ABB=ON  STAPHYLOCOCCUS AUREUS/CT
L18        3744 SEA FILE=CAPLUS ABB=ON  VIBRIO CHOLERAE/CT
L19        2146 SEA FILE=CAPLUS ABB=ON  SALMONELLA ENTERITIDIS/CT
L20       80199 SEA FILE=CAPLUS ABB=ON  INFECTION/CT
L21        2738 SEA FILE=CAPLUS ABB=ON  MASTITIS/CT
L22       50328 SEA FILE=CAPLUS ABB=ON  ANTIBACTERIAL AGENTS/CT
L23        4983 SEA FILE=CAPLUS ABB=ON  COLONIZ?/OBI
L24       22200 SEA FILE=CAPLUS ABB=ON  ANTIMICROBIAL AGENTS/CT
L25        8625 SEA FILE=CAPLUS ABB=ON  MICROBE#/OBI
L26      340478 SEA FILE=CAPLUS ABB=ON  MICROBIAL/OBI
L27       25812 SEA FILE=CAPLUS ABB=ON  VIRULENCE/CW
L28       13036 SEA FILE=CAPLUS ABB=ON  BIOFILM#/OBI
L30          70 SEA FILE=CAPLUS ABB=ON  L14 AND (PY<2004 OR AY<2004 OR
                PRY<2004)
L32      394845 SEA FILE=CAPLUS ABB=ON  BACTERI?/OBI
L33           5 SEA FILE=CAPLUS ABB=ON  L30 AND (L17 OR L18 OR L19 OR L20 OR
                L21 OR L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L32)



L8              STR
L13         136 SEA FILE=REGISTRY SSS FUL L8
```

```
L14          149 SEA FILE=CAPLUS ABB=ON  L13
L30           70 SEA FILE=CAPLUS ABB=ON  L14 AND (PY<2004 OR AY<2004 OR
                 PRY<2004)
L34           15 SEA FILE=CAPLUS ABB=ON  L14(L)(THU OR BAC OR PAC OR PKT OR
                 DMA)/RL       ROLES: THU=THERAPEUTIC USE; BAC=BIOLOGICAL ACTIVITY;
PAC=PHARMACOLOGIC ACTIVITY; PKT=PHARMACOKINETICS; DMA=DRUG MECHANISM OF ACTION
L35            6 SEA FILE=CAPLUS ABB=ON  L34 AND L30



L8               STR
L13          136 SEA FILE=REGISTRY SSS FUL L8
L14          149 SEA FILE=CAPLUS ABB=ON  L13
L30           70 SEA FILE=CAPLUS ABB=ON  L14 AND (PY<2004 OR AY<2004 OR
                 PRY<2004)
L36      2343963 SEA FILE=CAPLUS ABB=ON  PHARMAC?/SC,SX
L37            4 SEA FILE=CAPLUS ABB=ON  L30 AND L36



L8               STR
L13          136 SEA FILE=REGISTRY SSS FUL L8
L14          149 SEA FILE=CAPLUS ABB=ON  L13
L30           70 SEA FILE=CAPLUS ABB=ON  L14 AND (PY<2004 OR AY<2004 OR
                 PRY<2004)
L38       122405 SEA FILE=CAPLUS ABB=ON  IMPLANT?/OBI
L39        51350 SEA FILE=CAPLUS ABB=ON  PROSTHE?/OBI
L40       222938 SEA FILE=CAPLUS ABB=ON  DRUG DELIVERY SYSTEMS+OLD/CT
L41            1 SEA FILE=CAPLUS ABB=ON  L30 AND (L38 OR L39 OR L40)


=> s l33,l35,l37,l41 not l16,l82; fil medl; d que nos l45; s l45 not l47
L92           10 (L33 OR L35 OR L37 OR L41) NOT (L16 OR L82)  L16 & L82 WERE PRINTED
                                                              WITH INVENTOR SEARCH


FILE 'MEDLINE' ENTERED AT 15:37:40 ON 19 MAR 2008

 FILE LAST UPDATED: 18 Mar 2008 (20080318/UP).  FILE COVERS 1949 TO DATE.

  MEDLINE has been updated with the National Library of Medicine's
  revised 2008 MeSH terms.  See HELP RLOAD for details.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


L8               STR
L13          136 SEA FILE=REGISTRY SSS FUL L8
L43            2 SEA FILE=REGISTRY ABB=ON  L13 AND MEDLINE/LC
L44           79 SEA FILE=MEDLINE ABB=ON  L43
L45           17 SEA FILE=MEDLINE ABB=ON  L44 AND PY<2004



L93           17 L45 NOT L47    L47 WAS PRINTED WITH INVENTOR SEARCH

=> dup rem l92,l93
FILE 'CAPLUS' ENTERED AT 15:37:59 ON 19 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
```

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'MEDLINE' ENTERED AT 15:37:59 ON 19 MAR 2008
PROCESSING COMPLETED FOR L92
PROCESSING COMPLETED FOR L93
L94 23 DUP REM L92 L93 (4 DUPLICATES REMOVED)
ANSWERS '1-10' FROM FILE CAPLUS
ANSWERS '11-23' FROM FILE MEDLINE

=> d ibib abs hitind hitstr 1-10; d iall 11-23

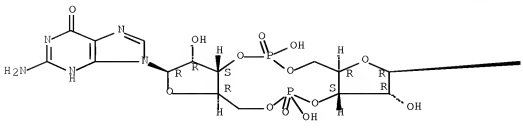
L94 ANSWER 1 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 1999:129234 CAPLUS Full-text
DOCUMENT NUMBER: 130:279806
TITLE: Elevated expression of the CD4 receptor and cell cycle arrest are induced in Jurkat cells by treatment with the novel cyclic dinucleotide 3',5'-cyclic diguanylic acid
AUTHOR(S): Steinberger, Osnat; Lapidot, Ziva; Ben-Ishai, Zvi; Amikam, Dorit
CORPORATE SOURCE: Molecular Oncology Laboratory, Rambam Medical Center and Rappaport Institute of Medical Sciences, Haifa, 31096, Israel
SOURCE: FEBS Letters (1999), 444(1), 125-129
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of the novel, naturally occurring nucleotide cyclic diguanylic acid (c-di-GMP) on the lymphoblastoid CD4+ Jurkat cell line was studied. When exposed to 50 μM c-di-GMP, Jurkat cells exhibited a markedly elevated expression of the CD4 receptor of up to 6.3-fold over controls. C-di-GMP also causes blockage of the cell cycle at the S-phase, characterized by increased cellular thymidine uptake, reduction in G2/M-phase cells, increase in S-phase cells and decreased cell division. Addnl. c-di-GMP naturally enters these cells and binds irreversibly to the P21ras protein. The effects described appear to be unique for c-di-GMP.

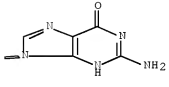
CC 13-6 (Mammalian Biochemistry)
IT 61093-23-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(elevated expression of CD4 receptor and cell cycle arrest are induced in Jurkat cells by treatment with novel cyclic dinucleotide 3',5'-cyclic diguanylic acid)
IT 61093-23-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(elevated expression of CD4 receptor and cell cycle arrest are induced in Jurkat cells by treatment with novel cyclic dinucleotide 3',5'-cyclic diguanylic acid)
RN 61093-23-0 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L94 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 1998:584586 CAPLUS Full-text
DOCUMENT NUMBER: 129:298869
TITLE: Three cdg operons control cellular turnover of cyclic di-GMP in Acetobacter xylinum: genetic organization and occurrence of conserved domains in isoenzymes
AUTHOR(S): Tal, Rony; Wong, Hing C.; Calhoon, Roger; Gelfand, David; Fear, Anna Lisa; Volman, Gail; Mayer, Raphael; Ross, Peter; Amikam, Dorit; Weinhouse, Haim; Cohen, Avital; Sapir, Shai; Ohana, Patricia; Benziman, Moshe
CORPORATE SOURCE: Cetus Corporation, Emeryville, CA, 94608, USA
SOURCE: Journal of Bacteriology (1998), 180(17), 4416-4425
CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cyclic di-GMP (c-di-GMP) is the specific nucleotide regulator of β-1,4-glucan (cellulose) synthase in Acetobacter xylinum. The enzymes controlling turnover of c-di-GMP are diguanylate cyclase (DGC), which catalyzes its formation, and phosphodiesterase A (PDEA), which catalyzes its degradation Following biochem. purification of DGC and PDEA, genes encoding isoforms of these enzymes have been isolated and found to be located on three distinct yet highly homologous operons for cyclic diguanylate, cdg1, cdg2, and cdg3. Within each cdg operon, a pdeA gene lies upstream of a dgc gene. Cdg1 contains two addnl. flanking genes, cdg1a and cdg1d. Cdg1a encodes a putative transcriptional activator, similar to AadR of Rhodopseudomonas palustris and FixK proteins of rhizobia. The deduced DGC and PDEA proteins have an identical motif structure of two lengthy domains in their C-terminal regions. These domains are also present in numerous bacterial proteins of undefined function. The N termini of the DGC and PDEA deduced proteins contain putative oxygen-sensing domains, based on similarity to domains on bacterial NifL and FixL proteins, resp. Genetic disruption analyses demonstrated a physiol. hierarchy among the cdg operons, such that cdg1 contributes 80% of cellular

DGC and PDEA activities and cdg2 and cdg3 contribute 15 and 5%, resp. Disruption of dgc genes markedly reduced in vivo cellulose production, demonstrating that c-di-GMP controls this process.

CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 7, 10

IT Gene, microbial
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(cbgla; three cdg operons control cellular turnover of cyclic di-GMP in Acetobacter xylinum: genetic organization and occurrence of conserved domains in isoenzymes)

IT Gene, microbial
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(cbgld; three cdg operons control cellular turnover of cyclic di-GMP in Acetobacter xylinum: genetic organization and occurrence of conserved domains in isoenzymes)

IT Gene, microbial
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(dgc; three cdg operons control cellular turnover of cyclic di-GMP in Acetobacter xylinum: genetic organization and occurrence of conserved domains in isoenzymes)

IT Gene, microbial
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(pdeA; three cdg operons control cellular turnover of cyclic di-GMP in Acetobacter xylinum: genetic organization and occurrence of conserved domains in isoenzymes)

IT 61093-23-0
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(three cdg operons control cellular turnover of cyclic di-GMP in Acetobacter xylinum: genetic organization and occurrence of conserved domains in isoenzymes)

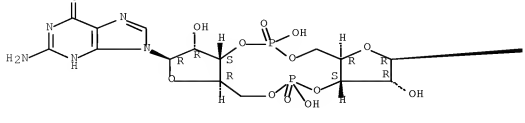
IT 61093-23-0
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(three cdg operons control cellular turnover of cyclic di-GMP in Acetobacter xylinum: genetic organization and occurrence of conserved domains in isoenzymes)

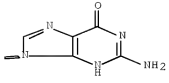
RN 61093-23-0 CAPLUS

CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L94 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 1995:912308 CAPLUS Full-text
DOCUMENT NUMBER: 124:51450
TITLE: The novel cyclic dinucleotide 3'-5' cyclic diguanylic acid binds to p21ras and enhances DNA synthesis but not cell replication in the Molt 4 cell line
AUTHOR(S): Amikam, Dorit; Steinberger, Osnat; Shkolnik, Tamar; Ben-Ishai, Zvi
CORPORATE SOURCE: Molecular Genetics Unit, Rambam Medical Center, Haifa, Israel
SOURCE: Biochemical Journal (1995), 311(3), 921-7
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of the novel, naturally occurring nucleotide 3'-5' cyclic diguanylic acid (c-di-GMP) on the lymphoblastoid Molt 4 cell line was studied. When exposed to this guanine nucleotide, Molt 4 cells exhibited a marked increase in [3H]thymidine incorporation, up to 200-fold at 50 μM c-di-GMP. Correspondingly, the DNA content of the treated cells was 9-fold higher than untreated cells. Stimulation of [3H]thymidine incorporation into the cells was time- and concentration-dependent. This effect was specific and was not observed with GMP or cGMP, nor with the unhydrolyzable GTP analogs, guanosine 5'-[γ-thio]triphosphate and guanosine 5'-[βγ-imido]triphosphate. C-di-GMP entrance into the cells was exptl. verified and occurred without using any means of cell permeabilization. SDS-PAGE anal. of cells exposed to [32P]c-di-GMP, followed by autoradiog., revealed the labeling of three low-mol.-mass proteins at 18-27 kDa. The labeling is highly specific to c-di-GMP and its extent was not affected by other guanine nucleotides. One of the c-di-GMP-binding proteins was the p21ras protein, by immunopptn. with the anti-Ras monoclonal antibody Y13-259. The effects described appear to be unique for c-di-GMP and, taken together, raise the possibility that an irreversible binding of this guanine nucleotide to the growth-promoting p21ras protein results in a fixed active conformation of this protein affecting DNA synthesis. Strikingly, although at 48 h of growth markedly high DNA levels were found in Molt 4 cells treated with c-di-GMP, this guanine nucleotide had no effect on cell replication during this period. Thus Molt 4 cells exposed to c-di-GMP enter the S phase uncoordinated with their overall replication rate.

CC 13-2 (Mammalian Biochemistry)
IT 61093-23-0
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cyclic diguanylic acid binding to p21ras and effect on DNA formation

and cell replication in lymphoblast)

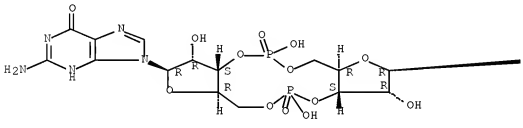
IT 61093-23-0
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cyclic diguanylic acid binding to p21ras and effect on DNA formation and cell replication in lymphoblast)

RN 61093-23-0 CAPLUS

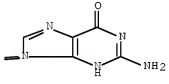
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L94 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 1983:13555 CAPLUS Full-text

DOCUMENT NUMBER: 98:13555

ORIGINAL REFERENCE NO.: 98:2181a,2184a

TITLE: RNA polymerase: linear competitive inhibition by bis-(3'→5')-cyclic dinucleotides, cyclic NpNp

AUTHOR(S): Hsu, Chin Yi Jenny; Dennis, Don

CORPORATE SOURCE: Dep. Chem., Univ. Delaware, Newark, DE, 19711, USA

SOURCE: Nucleic Acids Research (1982), 10(18), 5637-47
CODEN: NARHAD; ISSN: 0305-1048

DOCUMENT TYPE: Journal

LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB The possible role of bis-(3'→5')-cyclic di(uridine monophosphate) (I) and bis-(3'→5')-cyclic uridylyladenylate (II) as kinetic inhibitors of the DNA-dependent RNA polymerase of Escherichia coli was studied with T7ΔD111 deletion mutant DNA and several synthetic DNA polymers as templates. I is a linear competitive inhibitor of the initiation phase of the polymerization (Ki = 28 μM with T7ΔD111 DNA as a template), but it has no effect when added during the elongation phase. II is an inhibitor of the reaction only when poly(dA-

T)·poly(dA-T) is used as a template, and I is an inhibitor of the reaction when poly(dA)·poly(dT) was employed as the DNA template.

CC 7-3 (Enzymes)

IT Virus, bacteriai
(T7, DNA of mutant of, as RNA polymerase template, cyclic dinucleotide inhibition in relation to)

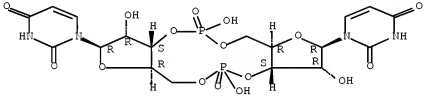
IT 73120-97-5 83799-66-0
RL: BIOL (Biological study)
(RNA polymerase of Escherichia coli inhibition by, elongation and initiation phases in relation to)

IT 73120-97-5 83799-66-0
RL: BIOL (Biological study)
(RNA polymerase of Escherichia coli inhibition by, elongation and initiation phases in relation to)

RN 73120-97-5 CAPLUS

CN 3'-Uridylic acid, uridylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

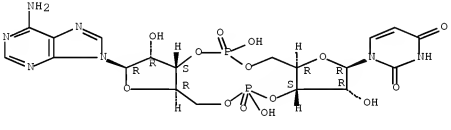
Absolute stereochemistry.



RN 83799-66-0 CAPLUS

CN 3'-Adenylic acid, uridylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L94 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:58224 CAPLUS Full-text

DOCUMENT NUMBER: 142:156269

TITLE: Method of synthesizing cyclic dinucleotide

INVENTOR(S): Hayakawa, Yoshihiro

PATENT ASSIGNEE(S): Mitsui Chemicals, Inc., Japan

SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005005450	A1	20050120	WO 2004-JP7000	20040517 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1645561	A1	20060412	EP 2004-733482	20040517 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2006167241	A1	20060727	US 2006-564476	20060113 <--
PRIORITY APPLN. INFO.:			JP 2003-274389	A 20030715 <--
			WO 2004-JP7000	W 20040517

OTHER SOURCE(S): MARPAT 142:156269
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A compound represented by the general formula (I) (wherein R2, R3 = H, halo, OMe, 2-methoxyethoxy, HO; B2, B3 = a nucleic acid base) or a salt thereof can be synthesized from a compound represented by the general formula (II) (wherein R1 = H, halo, OMe, 2-methoxyethoxy, HO substituted by a hydroxy-protecting group; B1 = an optionally protected nucleic acid base). Cyclic bis(3'→5')dinucleotide I is useful as an anticancer agent (no data). Thus, N2-(allyloxycarbonyl)-O6-allyl-2'-O-(tert- butyldimethylsilyl)-5'-O-(4,4'-dimethoxytrityl)guanosine 3'-O-(allyl N,N-diisopropylphosphoramidite) (III) was condensed with 2-cyanoethanol in the presence of imidazolium perchlorate and mol. sieve 3A in MeCN followed by treatment with imidazolium perchlorate for oxidation and then with dichloroacetic acid in CH2Cl2 for deprotection of 4,4'-dimethoxytrityl group gave guanosine phosphate triester (IV) (R = CH2CH2CN) which was similarly coupled with III to give dinucleotide IV (R = Q). IV (R = Q) was stirred with a mixture of 28% aqueous NH3 and MeOH at room temperature for 30 min, concentrated under reduced pressure, taken up in toluene three times and each time concentrated under reduced pressure, dissolved in THF, treated with N-methylimidazole and triisopropylbenzenesulfonyl chloride, and stirred at room temperature for 20 h to give protected cyclic dinucleotide (V) which was deprotected by treatment with Ph3P, n-butylamine, formic acid, and Pd2[(C6H4CH:CH)2CO]3.CHCl3 in THF at room temperature for 10 min and then with Et3N.3HF complex at room temperature for 12 h to give cyclic diguanylate I (B2 = B3 = guanine residue).

IC ICM C07H021-02
ICS C07H019-20; C07H019-10

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1

IT 61693-23-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(method of synthesizing anticancer cyclic dinucleotide and intermediates thereof)

IT 126922-61-0P 149559-87-5P 609343-79-5P 609343-80-8P
609343-81-9P 827602-95-9P 827602-96-0P 827602-97-1P
827602-98-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method of synthesizing anticancer cyclic dinucleotide and intermediates thereof)

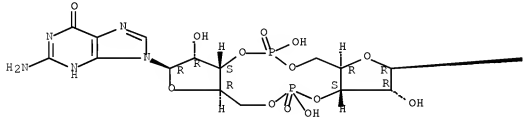
IT 61093-23-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of synthesizing anticancer cyclic dinucleotide and intermediates thereof)

RN 61093-23-0 CAPLUS

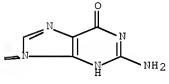
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



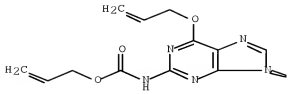
IT 609343-81-9P 827602-98-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method of synthesizing anticancer cyclic dinucleotide and intermediates thereof)

RN 609343-81-9 CAPLUS

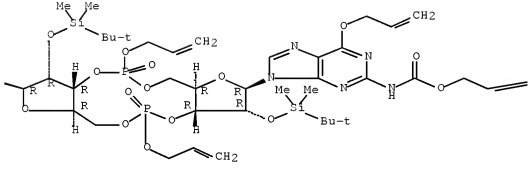
CN 3'-Guanylic acid, 2'-O-[(1,1-dimethylethyl)dimethylsilyl]-P-2-propenyl-6-O-2-propenyl-N-[(2-propenyloxy)carbonyl]guanylyl-(3'→5')-2'-O-[(1,1-dimethylethyl)dimethylsilyl]-6-O-2-propenyl-N-[(2-propenyloxy)carbonyl]-, mono-2-propenyl ester, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

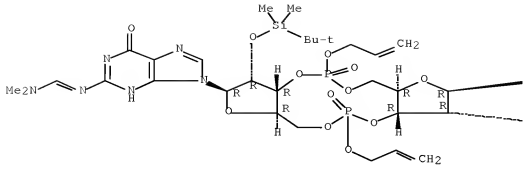


PAGE 1-C

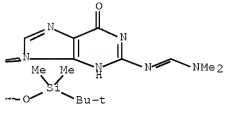
RN 827602-98-2 CAPLUS
CN 3'-Guanylic acid, 2'-O-[(1,1-dimethylethyl)dimethylsilyl]-N-[(dimethylamino)methylene]-P-2-propenylguanylyl-(3'→5')-2'-O-[(1,1-dimethylethyl)dimethylsilyl]-N-[(dimethylamino)methylene]-, mono-2-propenyl ester, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L94 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:272942 CAPLUS Full-text
DOCUMENT NUMBER: 126:340371
TITLE: Probing interactions between viral DNA and human immunodeficiency virus type 1 integrase using dinucleotides
AUTHOR(S): Mazumder, Abhijit; Uchida, Hiroyuki; Neamati, Nouri; Sunder, Sanjay; Jaworska-Maslanka, Maria; Wickstrom, Eric; Zeng, Fan; Jones, Roger A.; Mandes, Robert F.; et al.
CORPORATE SOURCE: Laboratories of Molecular Pharmacology, Division of Basic Sciences, Medicine Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Molecular Pharmacology (1997), 51(4), 567-575
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Retroviral integrases are essential for viral replication and represent an attractive chemotherapeutic target. In the current study, we demonstrated the activity of micromolar concns. of dinucleotides against human immunodeficiency virus type 1 (HIV-1), HIV type 2 (HIV-2), simian immunodeficiency virus, and feline immunodeficiency virus integrases. The structure-activity relationship indicates that 5'-phosphorylation enhances potency and that phosphodiester and

sugar modifications affect the inhibition of HIV-1 integrase. Base sequence selectivity was observed: pAC, pAT, and pCT were the most potent inhibitors, whereas pAA, pGA, and pGC showed low activity at 100 μM. The inhibition by pAC is consistent with the interaction of the enzyme with the 5' end of the noncleaved strand (5'-AC-3'). The linear and cyclic dinucleotides released by the 3'-processing reaction did not affect enzymic activity at physiol. concns. An increase in the length to trinucleotides or tetranucleotides enhanced potency by only 2-3-fold, suggesting that two neighboring bases may be sufficient for significant interactions. Inhibition of a truncated (50-212) integrase mutant and global inhibition of all nucleophiles in the 3'-processing reaction suggest that dinucleotides bind in the catalytic core. All of the active dinucleotides inhibited enzyme/DNA binding in their resp. IC50 range. Although the dinucleotides tested showed no antiviral activity, these observations demonstrate the usefulness of dinucleotides in elucidating enzyme mechanisms and as potential ligands for cocrystn. and as lead structures for development of antivirals.

CC 7-3 (Enzymes)

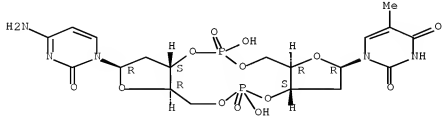
IT 2147-10-6 2147-15-1 2382-66-3 2402-35-9 2642-45-7 4251-24-5
4336-86-1 4353-69-9 4398-09-8 4568-39-2 4568-41-6
4568-42-7 4624-07-1 15561-99-6 15562-00-2 15623-43-5
16240-63-4 25324-45-2 26467-02-7 26467-04-9 28267-23-4
38665-19-9 38665-20-2 38976-21-5 47905-67-9 49835-11-2
58459-15-7 60307-63-3 79192-34-0 82739-97-7
109699-00-5 129185-16-6 134247-05-5 189883-56-5
189883-57-6 189883-58-7 189883-59-8 189883-60-1 189883-61-2
189883-62-3 189883-63-4 189883-64-5 189883-65-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(probing interactions between viral DNA and human immunodeficiency virus type 1 integrase using dinucleotides)

IT 4568-39-2 4568-41-6 4568-42-7
25324-45-2 60307-63-3 79192-34-0
109699-00-5 129185-16-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(probing interactions between viral DNA and human immunodeficiency virus type 1 integrase using dinucleotides)

RN 4568-39-2 CAPLUS

CN 3'-Thymidylic acid, 2'-deoxycytidylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

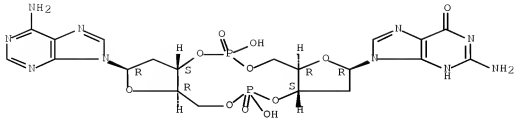
Absolute stereochemistry.



RN 4568-41-6 CAPLUS

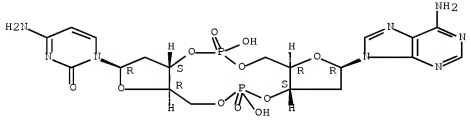
CN 3'-Guanylic acid, 2'-deoxyadenylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



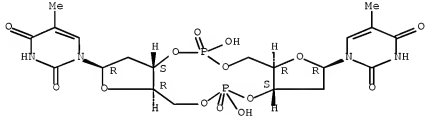
RN 4568-42-7 CAPLUS
CN 3'-Adenylic acid, 2'-deoxycytidylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 25324-45-2 CAPLUS
CN 3'-Thymidylic acid, thymidylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

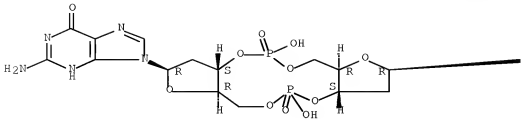
Absolute stereochemistry.



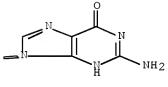
RN 60307-63-3 CAPLUS
CN 3'-Guanylic acid, 2'-deoxyguanylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



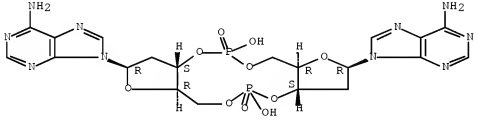
PAGE 1-B



RN 79192-34-0 CAPLUS

CN 3'-Adenylic acid, 2'-deoxyadenylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

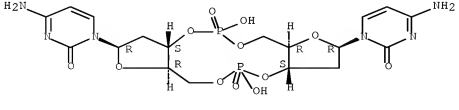
Absolute stereochemistry.



RN 109699-00-5 CAPLUS

CN 3'-Cytidylic acid, 2'-deoxycytidylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

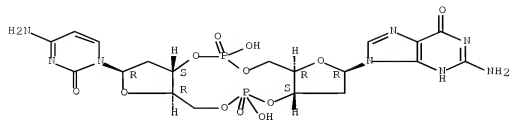


RN 129185-16-6 CAPLUS

CN 3'-Guanylic acid, 2'-deoxycytidylyl-(3'→5')-2'-deoxy-, cyclic

nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L94 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:553377 CAPLUS Full-text
DOCUMENT NUMBER: 119:153377
TITLE: Cloning of cyclic di-guanylate metabolic enzymes of Acetobacter xylinum
INVENTOR(S): Tal, Rony; Gelfand, David H.; Calhoon, Roger D.; Ben-Bassat, Arie; Benziman, Moshe; Wong, Hing Cheung
PATENT ASSIGNEE(S): Weyerhaeuser Co., USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9311244	A1	19930610	WO 1992-US8756	19921014 <--
W: JP, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
EP 620852	A1	19941026	EP 1992-921754	19921014 <--
R: DE, DK, FR, GB, NL				
JP 07501450	T	19950216	JP 1992-510095	19921014 <--
US 5759828	A	19980602	US 1994-309512	19940920 <--
PRIORITY APPLN. INFO.:			US 1991-800218 A	19911129 <--
			WO 1992-US8756 W	19921014 <--

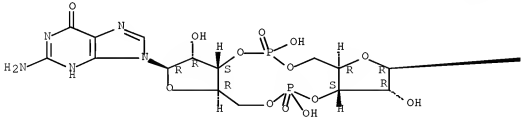
AB The cdg1, cdg2, and cdg3 operons of A. xylinum are cloned and sequenced. Cyclic diguanosine monophosphate is an activator of cellulose synthase. The 3 operons contain genes encoding diguanylate cyclase (dgc genes) and genes encoding cyclic diguanosine monophosphate phosphodiesterase A (pdeA genes). A. xylinum containing inactivating mutations in dgc or pdeA genes were prepared and the activity of the various enzymes was determined

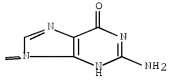
IC ICM C12N015-52
ICS C12N015-55; C12N015-60; C07K015-00; C12N001-20
ICA C12P019-04
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 7
IT Gene, microbial
RL: BIOL (Biological study)
(cdg1D, of Acetobacter xylinum, cloning and sequence of)
IT Gene, microbial

RL: BIOL (Biological study)
(cdg1A, of Acetobacter xylinum, cloning and sequence of)
IT Gene, microbial
RL: BIOL (Biological study)
(dgc1, for diguanylate cyclase of Acetobacter xylinum, cloning and sequence of)
IT Gene, microbial
RL: BIOL (Biological study)
(dgc2, for diguanylate cyclase of Acetobacter xylinum, cloning and sequence of)
IT Gene, microbial
RL: BIOL (Biological study)
(dgc3, for diguanylate cyclase of Acetobacter xylinum, cloning and sequence of)
IT Gene, microbial
RL: BIOL (Biological study)
(pdeA1, for cyclic diguanosine monophosphate phosphodiesterase A of Acetobacter xylinum, cloning and sequence of)
IT Gene, microbial
RL: BIOL (Biological study)
(pdeA2, for cyclic diguanosine monophosphate phosphodiesterase A of Acetobacter xylinum, cloning and sequence of)
IT Gene, microbial
RL: BIOL (Biological study)
(pdeA3, for cyclic diguanosine monophosphate phosphodiesterase A of Acetobacter xylinum, cloning and sequence of)
IT 61093-23-0
RL: BIOL (Biological study)
(enzymes metabolizing, of Acetobacter xylinum, cloning and sequencing of cdg operons encoding)
IT 61093-23-0
RL: BIOL (Biological study)
(enzymes metabolizing, of Acetobacter xylinum, cloning and sequencing of cdg operons encoding)
RN 61093-23-0 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

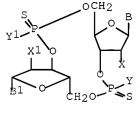




L94 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:671631 CAPLUS Full-text
DOCUMENT NUMBER: 119:271631
TITLE: Cyclic oligonucleotide phosphorothioates
INVENTOR(S): Battistini, Carlo; Fustinoni, Silvia; Brasca, Maria Gabriella; Ungheri, Domenico
PATENT ASSIGNEE(S): Farmitalia Carlo Erba S.r.l., Italy
SOURCE: Ger. Offen., 20 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4223438	A1	19930121	DE 1992-4223438	19920716 <--
GB 2257704	A	19930120	GB 1991-15586	19910718 <--
GB 2257704	B	19950301		
JP 05186495	A	19930727	JP 1992-191152	19920717 <--
US 5547941	A	19960820	US 1994-354888	19941209 <--
PRIORITY APPLN. INFO.:			GB 1991-15586 A	19910718 <--
			US 1992-914923 B1	19920717 <--
OTHER SOURCE(S):	MARPAT 119:271631			

GI



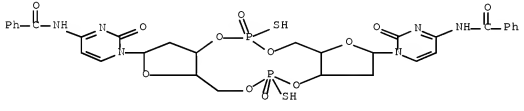
I

AB Title compds. I (B, B1 = nucleic acid base; X, X1 = H, F, OH, alkoxy; Y, Y1 = H, SH, OH) were prepared as virucides. Thus, (Rp,Rp)- and (Sp,Rp)-I (B, B1 = cytosine, X, X1 = H, Y, Y1 = ONa) were prepared from protected deoxycytidine in 5 steps. At 10μM (Rp,Rp)-I (B, B1 = cytosine, X, X1 = H, Y, Y1 = ONa) inhibited HIV replication at both the protein and the RNA level for 3 days.
IC ICM C07H019-10
ICS A61K031-70
CC 33-9 (Carbohydrates)
Section cross-reference(s): 1

IT 148473-28-3 148504-39-6 148555-08-2 148555-87-7
148555-92-4 148555-94-6 149496-20-8 149496-22-0 149713-32-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(intermediate for virucidal dinucleotide cyclic phosphorothioates)
IT 147975-79-9 149496-26-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation as virucide)
IT 147975-80-2P 147975-81-3P 148555-07-1P 148555-89-9P
148555-91-3P 148555-93-5P 149416-61-5P 149496-23-1P
149496-24-2P 149496-27-5P 149496-28-6P 149496-29-7P
149559-84-2P 149656-73-5P 151330-52-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT 148555-08-2 149713-32-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(intermediate for virucidal dinucleotide cyclic phosphorothioates)
RN 148555-08-2 CAPLUS
CN Cytidine, [P(R)]-N-benzoyl-2'-deoxy-P-thiocytidylyl-(3'→5')-N-benzoyl-2'-deoxy-, 3'-[dihydrogen [P(S)]-phosphorothioate], cyclic nucleotide, compd. with N,N-diethylethanamine (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 148555-07-1
CMF C32 H32 N6 O12 P2 S2



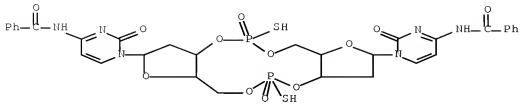
CM 2

CRN 121-44-8
CMF C6 H15 N

RN 149713-32-6 CAPLUS
CN Cytidine, [P(R)]-N-benzoyl-2'-deoxy-P-thiocytidylyl-(3'→5')-N-benzoyl-2'-deoxy-, 3'-[dihydrogen [P(R)]-phosphorothioate), cyclic nucleotide, compd. with N,N-diethylethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 149656-73-5
CMF C32 H32 N6 O12 P2 S2

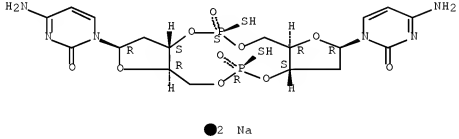


CM 2

CRN 121-44-8
CMF C6 H15 N

IT 147975-79-9 149496-26-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation as virucide)
RN 147975-79-9 CAPLUS
CN Cytidine, [P(R)]-2'-deoxy-P-thiocytidylyl-(3'→5')-2'-deoxy-,
3'-[dihydrogen [P(S)]-phosphorothioate], cyclic nucleotide, disodium salt
(9CI) (CA INDEX NAME)

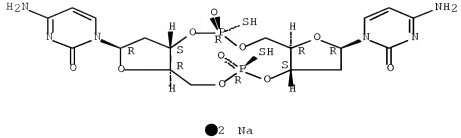
Absolute stereochemistry.



Absolute stereochemistry.

RN 149496-26-4 CAPLUS
CN Cytidine, [P(R)]-2'-deoxy-P-thiocytidylyl-(3'→5')-2'-deoxy-,
3'-[dihydrogen [P(R)]-phosphorothioate], cyclic nucleotide, disodium salt
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

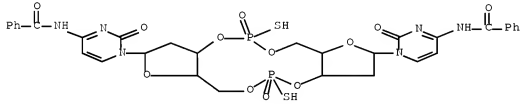


●2 Na

IT 148555-07-1P 149416-61-5P 149496-27-5P
149559-84-2P 149656-73-5P 151380-52-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

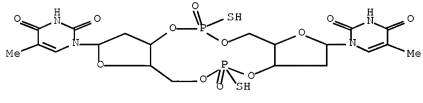
RN 148555-07-1 CAPLUS

CN Cytidine, [P(R)]-N-benzoyl-2'-deoxy-P-thiocytidylyl-(3'→5')-N-benzoyl-2'-deoxy-, 3'-[dihydrogen [P(S)]-phosphorothioate], cyclic nucleotide (9CI) (CA INDEX NAME)



RN 149416-61-5 CAPLUS

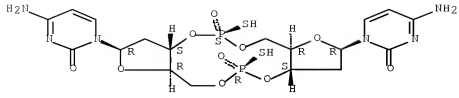
CN Thymidine, [P(R)]-P-thiothymidylyl-(3'→5')-, 3'-[dihydrogen [P(R)]-phosphorothioate], cyclic nucleotide (9CI) (CA INDEX NAME)



RN 149496-27-5 CAPLUS

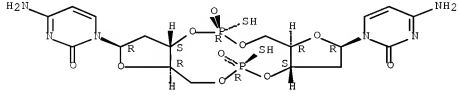
CN Cytidine, [P(R)]-2'-deoxy-P-thiocytidylyl-(3'→5')-2'-deoxy-, 3'-[dihydrogen [P(S)]-phosphorothioate], cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

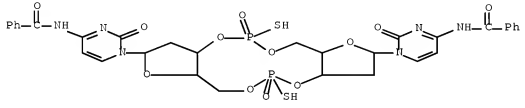


RN 149559-84-2 CAPLUS
CN Cytidine, [P(R)]-2'-deoxy-P-thiocytidylyl-(3'→5')-2'-deoxy-, 3'-[dihydrogen [P(R)]-phosphorothioate], cyclic nucleotide (9CI) (CA INDEX NAME)

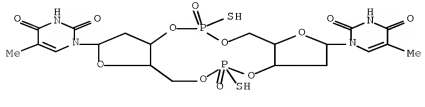
Absolute stereochemistry.



RN 149656-73-5 CAPLUS
CN Cytidine, [P(R)]-N-benzoyl-2'-deoxy-P-thiocytidylyl-(3'→5')-N-benzoyl-2'-deoxy-, 3'-[dihydrogen [P(R)]-phosphorothioate), cyclic nucleotide (9CI) (CA INDEX NAME)



RN 151380-52-8 CAPLUS
CN Thymidine, [P(R)]-P-thiothymidylyl-(3'→5')-, 3'-[hydrogen [P(S)]-phosphorothioate), cyclic nucleotide (9CI) (CA INDEX NAME)



L94 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:194777 CAPLUS Full-text

DOCUMENT NUMBER: 116:194777
TITLE: Synthesis of cyclic and acyclic oligocytidylates by uranyl ion catalyst in aqueous solution
AUTHOR(S): Sawai, Hiroaki; Higa, Katsutaka; Kuroda, Kensei
CORPORATE SOURCE: Fac. Eng., Gunma Univ., Kiryu, 376, Japan
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1992), (4), 505-8
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Uranyl ion catalyzes oligomerization of cytidine 5'-phosphoroimidazolide in aqueous solution, yielding (3'→5')-linked cyclic di- and tri-cytidylates preferentially at high catalyst concentration, or (2'→5')-linked linear oligocytidylates at lower catalyst concentration Addition of Ag+ affects the uranyl ion-catalyzed oligocytidylate formation and alters the product distribution.

CC 33-9 (Carbohydrates)

IT 9013-05-2, Phosphatase
RL: RCT (Reactant); RACT (Reactant or reagent)
(bacterial alkaline, hydrolysis of oligonucleotides in presence of)

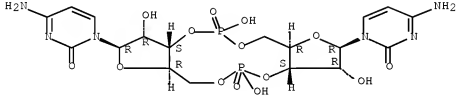
IT 55779-61-8P 73121-00-3P 73352-95-1P 84311-66-0P
84877-28-1P 84877-31-6P 140654-90-6P 140654-91-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, by uranyl ion-catalyzed oligomerization of cytidine phosphoroimidazolide)

IT 73121-00-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, by uranyl ion-catalyzed oligomerization of cytidine phosphoroimidazolide)

RN 73121-00-3 CAPLUS

CN 3'-Cytidylic acid, cytidylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L94 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1989:614862 CAPLUS Full-text
DOCUMENT NUMBER: 111:214862
TITLE: The cyclic dimer of 5-fluoro-2'-deoxyuridylic acid: a potent anticancer agent
AUTHOR(S): Hamoir, G.; Sonveaux, E.; Iigo, M.; De Clercq, E.
CORPORATE SOURCE: Lab. Biochim. Phys. Biopolym., Univ. Cathol. Louvain, Louvain-La-Neuve, B-1348, Belg.
SOURCE: Nucleosides & Nucleotides (1989), 8(2), 285-95
CODEN: NUNUD5; ISSN: 0732-8311

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:214862
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The cyclic dimer (I; U[5F] = 5-fluorouracil residue) of 5-fluoro-2'-deoxyuridylic acid (FdUMP) was synthesized. The fully protected dimer II (DMTr = 4,4'-dimethoxytrityl) was obtained following the phosphotriester strategy of J. C. Catlin and F. Cramer (1973). Autocondensation and deprotection then afforded the title compound I [cyclo(5FdUp5FdUp)] in excellent yield. In vitro, I proved slightly less active than FdUrd in inhibiting the proliferation of various murine and human tumor cells, but, in vivo, I was equally effective, and less toxic than 5-fluoro-2'-deoxyuridine in inhibiting adenocarcinoma tumor growth in mice.

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1

IT 123558-44-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, antitumor activity, and NMR of)

IT 123558-42-9P 123620-75-7P 123620-76-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, deprotection, and NMR of)

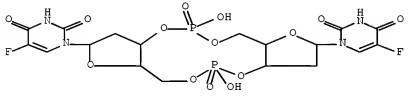
IT 123558-44-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, antitumor activity, and NMR of)

RN 123558-44-1 CAPLUS

CN 3'-Uridylic acid, 2'-deoxy-5-fluorouridylyl-(3'→5')-2'-deoxy-5-fluoro-, cyclic nucleotide, compd. with N,N-diethylethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

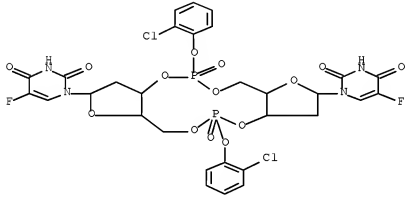
CRN 123558-43-0
CMF C18 H20 F2 N4 O14 P2



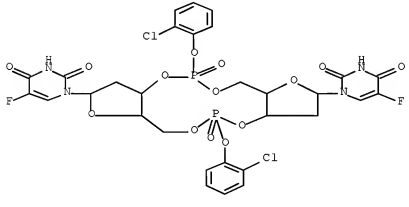
CM 2

CRN 121-44-8
CMF C6 H15 N

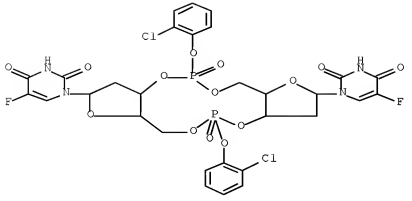
IT 123558-42-9P 123620-75-7P 123620-76-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, deprotection, and NMR of)
RN 123558-42-9 CAPLUS
CN 3'-Uridylic acid, (R)-P-(2-chlorophenyl)-2'-deoxy-5-fluorouridylyl-(3'→5')-2'-deoxy-5-fluoro-, cyclic nucleotide, 2-chlorophenyl ester, (R)- (9CI) (CA INDEX NAME)



RN 123620-75-7 CAPLUS
CN 3'-Uridylic acid, (S)-P-(2-chlorophenyl)-2'-deoxy-5-fluorouridylyl-(3'→5')-2'-deoxy-5-fluoro-, cyclic nucleotide, 2-chlorophenyl ester, (S)- (9CI) (CA INDEX NAME)



RN 123620-76-8 CAPLUS
CN 3'-Uridylic acid, (R)-P-(2-chlorophenyl)-2'-deoxy-5-fluorouridylyl-(3'→5')-2'-deoxy-5-fluoro-, cyclic nucleotide, 2-chlorophenyl ester, (S)- (9CI) (CA INDEX NAME)



L94 ANSWER 11 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2003448676 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14510401
TITLE: A new synthetic approach to cyclic bis(3'-->5')diguanylic acid.
AUTHOR: Kawai Rie; Nagata Reiko; Hirata Akiyoshi; Hayakawa Yoshihiro
CORPORATE SOURCE: Graduate School of Human Informatics, Nagoya University, Chikusa, Nagoya 464-8601, Japan.
SOURCE: Nucleic acids research. Supplement (2001), (2003) No. 3, pp. 103-4.
Journal code: 101169367.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 28 Sep 2003
Last Updated on STN: 1 Nov 2003
Entered Medline: 31 Oct 2003
ABSTRACT:
We developed a novel synthesis of biologically important cyclic bis(3'-->5')diguanylic acid (cGpGp). The present synthesis includes two strategies different from those employed in an existing synthesis. They are the phosphoramidite method for the preparation of a guanylyl(3'-->5')guanylic acid intermediate and allyl protection for guanine bases and internucleotide linkages. These distinctive strategies have allowed the new synthesis to provide the target compound in a higher yield than that of the existing synthesis.
CONTROLLED TERM: *Cyclic GMP: AA, analogs & derivatives
*Cyclic GMP: CS, chemical synthesis
Cyclic GMP: CH, chemistry
Nuclear Magnetic Resonance, Biomolecular
Spectrometry, Mass, Electrospray Ionization
CAS REGISTRY NO.: 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7665-99-8 (Cyclic GMP)

L94 ANSWER 12 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2001495621 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 11544230
TITLE: Localization of c-di-GMP-binding protein with the linear terminal complexes of Acetobacter xylinum.
AUTHOR: Kimura S; Chen H P; Saxena I M; Brown R M Jr; Itoh T
CORPORATE SOURCE: Wood Research Institute, Kyoto University, Uji, Kyoto 611-0011, Japan.
SOURCE: Journal of bacteriology, (2001 Oct) Vol. 183, No. 19, pp. 5668-74.
Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 10 Sep 2001
Last Updated on STN: 15 Oct 2001
Entered Medline: 11 Oct 2001

ABSTRACT:
Specific labeling of a single row of cellulose-synthesizing complexes (terminal complexes, TC subunits, TCs, or TC arrays) in Acetobacter xylinum by antibodies raised against a 93-kDa protein (the cyclic dignanylic acid-binding protein) has been demonstrated by using the sodium dodecyl sulfate (SDS)-freeze-fracture labeling (FRL) technique. The antibodies to the 93-kDa protein specifically recognized the TC subunits on the protoplasmic fracture (PF) face of the outer membrane in A. xylinum; however, nonlabeled TCs were also observed. Two types of TC subunits (particles or pits) are observed on the PF face of the outer membrane: (i) immunogold-labeled TCs showing a line of depressions (pits) with an indistinct particle array and (ii) nonlabeled TC subunits with a distinct single row of particle arrays. The evidence indicates that the labeling patterns differ with respect to the presence or absence of certain TC subunits remaining attached to the replica after SDS treatment. This suggests the presence of at least two TC components, one in the outer membrane and the other in the cytoplasmic membrane. If the TC component in the outer membrane is preferentially fractured and remains attached to the ectoplasmic fracture face (or outer leaflet) of the outer membrane, subsequent replica formation reveals a pit or depression with positive antibody labeling on the PF face of the outer membrane. If the TC component in the outer membrane remains with the PF face (or inner leaflet) of the outer membrane, the innermost TC component is removed during SDS treatment and labeling does not occur. SDS-FRL of TCs in A. xylinum has enabled us to provide the first topological molecular analysis of component proteins in a cellulose-synthesizing TC structure in a prokaryotic organism.

CONTROLLED TERM: Bacterial Proteins: CH, chemistry
*Bacterial Proteins: ME, metabolism
Cyclic GMP: AA, analogs & derivatives
*Cyclic GMP: ME, metabolism
Freeze Fracturing: MT, methods
Gluconacetobacter xylinus: GD, growth & development
*Gluconacetobacter xylinus: ME, metabolism
Gluconacetobacter xylinus: UL, ultrastructure
Glucosyltransferases: CH, chemistry
*Glucosyltransferases: ME, metabolism
Immunohistochemistry
Microscopy, Electron
CAS REGISTRY NO.: 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7665-99-8 (Cyclic GMP)
CHEMICAL NAME: 0 (Bacterial Proteins); EC 2.4.1.- (Glucosyltransferases); EC 2.4.1.- (cellulose synthase (cyclic diguanylic acid))

L94 ANSWER 13 OF 23 MEDLINE on STN

ACCESSION NUMBER: 2001574658 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11682196
TITLE: Genetic data indicate that proteins containing the GGDEF domain possess diguanylate cyclase activity.
AUTHOR: Ausmees N; Mayer R; Weinhouse H; Volman G; Amikam D; Benziman M; Lindberg M
CORPORATE SOURCE: Department of Microbiology, Swedish University of Agricultural Sciences, SLU, Box 7025, S-75007 Uppsala, Sweden.. nora.ausmees@mikrob.slu.se
SOURCE: FEMS microbiology letters, (2001 Oct 16) Vol. 204, No. 1, pp. 163-7.
Journal code: 7705721. ISSN: 0378-1097.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 30 Oct 2001
Last Updated on STN: 25 Jan 2002
Entered Medline: 9 Jan 2002

ABSTRACT:
A conserved domain, called GGDEF (referring to a conserved central sequence pattern), is detected in many procaryotic proteins, often in various combinations with putative sensory-regulatory components. Most sequenced bacterial genomes contain several different GGDEF proteins. The function of this domain has so far not been experimentally shown. Through genetic complementation using genes from three different bacteria encoding proteins with GGDEF domains as the only element in common, we present genetic data indicating (a) that the GGDEF domain is responsible for the diguanylate cyclase activity of these proteins, and (b) that the activity of cellulose synthase in Rhizobium leguminosarum bv. trifolii and Agrobacterium tumefaciens is regulated by cyclic di-GMP as in Acetobacter xylinum.

CONTROLLED TERM: Amino Acid Motifs
*Bacterial Proteins: CH, chemistry
*Bacterial Proteins: GE, genetics
Bacterial Proteins: ME, metabolism
Cellulose: ME, metabolism
*Cyclic GMP: AA, analogs & derivatives
Cyclic GMP: ME, metabolism
Gene Expression Regulation, Bacterial
*Phosphorus-Oxygen Lyases: CH, chemistry
Phosphorus-Oxygen Lyases: GE, genetics
*Phosphorus-Oxygen Lyases: ME, metabolism
Plasmids: GE, genetics
Protein Structure, Tertiary
Repressor Proteins: CH, chemistry
Repressor Proteins: GE, genetics
Repressor Proteins: ME, metabolism
Rhizobium: EN, enzymology
Rhizobium: GE, genetics
CAS REGISTRY NO.: 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7665-99-8 (Cyclic GMP); 9004-34-6 (Cellulose)
CHEMICAL NAME: 0 (Bacterial Proteins); 0 (CelR protein, bacteria); 0 (PleD protein, Caulobacter crescentus); 0 (Repressor Proteins); EC 4.6.- (Phosphorus-Oxygen Lyases); EC 4.6.1.- (diguanylate cyclase)

L94 ANSWER 14 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1998034149 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 9369216
TITLE: c-di-GMP-binding protein, a new factor regulating cellulose synthesis in Acetobacter xylinum.
AUTHOR: Weinhouse H; Sapir S; Amikam D; Shilo Y; Volman G; Ohana P; Benziman M
CORPORATE SOURCE: Department of Biological Chemistry, Institute of Life Sciences, Hebrew University of Jerusalem, Givat Ram, Israel.
SOURCE: FEBS letters, (1997 Oct 20) Vol. 416, No. 2, pp. 207-11.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 9 Jan 1998
Last Updated on STN: 9 Jan 1998
Entered Medline: 8 Dec 1997

ABSTRACT:
A protein which specifically binds cyclic diguanylic acid (c-di-GMP), the reversible allosteric activator of the membrane-bound cellulose synthase system of Acetobacter xylinum, has been identified in membrane preparations of this organism. c-di-GMP binding is of high affinity (KD 20 nM), saturable and reversible. The equilibrium of the reaction is markedly and specifically shifted towards the binding direction by K+. The c-di-GMP binding protein, structurally associated with the cellulose synthase, appears to play a major role in modulating the intracellular concentration of free c-di-GMP and thus may constitute an essential factor in regulating cellulose synthesis in vivo.

CONTROLLED TERM: Allosteric Regulation
Bacterial Proteins: IP, isolation & purification
*Bacterial Proteins: ME, metabolism
Carrier Proteins: IP, isolation & purification
*Carrier Proteins: ME, metabolism
*Cellulose: BI, biosynthesis
Chromatography, Gel
*Cyclic GMP: AA, analogs & derivatives
Cyclic GMP: ME, metabolism
Energy Metabolism: DE, drug effects
Enzyme Activation
Ethanolamines: PD, pharmacology
*Gluconacetobacter xylinus: ME, metabolism
Glucosyltransferases: ME, metabolism
Kinetics
Potassium: PD, pharmacology
CAS REGISTRY NO.: 111-42-2 (diethanolamine); 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7440-09-7 (Potassium); 7665-99-8 (Cyclic GMP); 9004-34-6 (Cellulose)
CHEMICAL NAME: 0 (Bacterial Proteins); 0 (Carrier Proteins); 0 (Ethanolamines); EC 2.4.1.- (Glucosyltransferases); EC 2.4.1.- (cellulose synthase (cyclic diguanylic acid))

L94 ANSWER 15 OF 23 MEDLINE on STN
ACCESSION NUMBER: 96311792 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8758880
TITLE: Application of a self-modeling curve resolution approach to the study of solvent effects on the acid-base and copper (II)-complexing behavior of polyuridylic acid.
AUTHOR: de Juan A; Fonrodona G; Gargallo R; Izquierdo-Ridorsa A;

Tauler R; Casassas E
CORPORATE SOURCE: Departamento de Quimica Analitica, Universitat de Barcelona, Spain.
SOURCE: Journal of inorganic biochemistry, (1996 Aug 15) Vol. 63, No. 3, pp. 155-73.
Journal code: 7905788. ISSN: 0162-0134.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 15 Oct 1996
Last Updated on STN: 3 Feb 1997
Entered Medline: 2 Oct 1996

ABSTRACT:
The solvent effect on the acid-base and complexation behavior of the homopolynucleotide polyuridylic acid (poly(U)) has been studied by means of potentiometric and spectrometric titrations (circular dichroism and UV-VIS) in water and in 30 and 50% (v/v) dioxane-water media. The potentiometric studies revealed the absence of polyelectrolytic effects in the acid-base equilibrium, and the spectrometric experiments detected only a random coil conformation associated with both the protonated and deprotonated species. The common behavior observed in the three media seems to indicate the weakness of both intramolecular interactions, i.e., base stacking, and solute/solvent interactions, i.e., hydrogen-bonding, and consequently their small effect during the protonation process. Differences regarding the solubility of the deprotonated species in the solvents used are due to the difficult stabilization of such a charged species in the low polar environment of the dioxane-water mixtures. Complexation has been exhaustively studied in aqueous media, and no conformational changes have been noticed in the only copper(II)-poly(U) complex detected. The inclusion of the copper(II) ion in the macromolecular skeleton of the polynucleotide does not contribute to an ordination of the structure, which remains as a random coil. No comparison between this equilibrium in aqueous solution and in the hydroorganic mixtures could be carried out since the limited pH range of the soluble complex in those solvent mixtures prevented a rigorous quantitative monitoring of such a chemical process.

CONTROLLED TERM:
Acids: CH, chemistry
Base Sequence
Circular Dichroism
Copper: CH, chemistry
*Copper: ME, metabolism
Dioxanes
Least-Squares Analysis
Molecular Sequence Data
Nucleotides, Cyclic: CH, chemistry
*Poly U: CH, chemistry
Poly U: ME, metabolism
Potentiometry
Protons
*Solvents
Spectrophotometry: MT, methods
Titrimetry
Ultraviolet Rays
Water
CAS REGISTRY NO.: 123-91-1 (1,4-dioxane); 27416-86-0 (Poly U); 73128-97-5 (bis(3'-5')cyclic diuridine monophosphate) ; 7440-50-8 (Copper); 7732-18-5 (Water)

CHEMICAL NAME: 0 (Acids); 0 (Dioxanes); 0 (Nucleotides, Cyclic); 0 (Protons); 0 (Solvents)

L94 ANSWER 16 OF 23 MEDLINE on STN
ACCESSION NUMBER: 96439277 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8841612
TITLE: Synthesis of oligonucleotide having a bent structure by incorporation of an interresidually cyclized uridylyl (3'-5')uridine unit.
AUTHOR: Seio K; Wada T; Sekine M; Sakamoto K; Yokoyama S
CORPORATE SOURCE: Department of Life Science, Tokyo Institute of Technology, Yokomama, Japan.
SOURCE: Nucleic acids symposium series, (1995) No. 34, pp. 181-2.
Journal code: 8007206. ISSN: 0261-3166.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 28 Jan 1997
Last Updated on STN: 28 Jan 1997
Entered Medline: 18 Dec 1996

ABSTRACT:
The chemical synthesis and conformational properties of interresidually cyclized uridylyl(3'-5')uridine derivatives were studied in order to introduce a stable turn structure into oligonucleotides. These cyclized molecules were analogs of uridylyl(3'-5')5-[methylamino(methyl)]-uridine which is the component of the U turn structure of tRNAarg E. coli. The conformational properties of these cyclic dinucleoside monophosphates were studied using NMR and CD spectroscopy with the aid of molecular mechanics and molecular dynamics simulations. These experiments indicated that the turn conformation could be stabilized by introducing a cyclic structure as expected. On the basis of these results, the chemical synthesis of phosphoramidite units of these cyclic dinucleoside monophosphate derivatives were studied to construct oligonucleotides having a stable bent structure.

CONTROLLED TERM: Circular Dichroism
Computer Simulation
Dinucleoside Phosphates: CS, chemical synthesis
Dinucleoside Phosphates: CH, chemistry
Magnetic Resonance Spectroscopy
Molecular Structure
Nucleic Acid Conformation
*Nucleotides, Cyclic: CS, chemical synthesis
Nucleotides, Cyclic: CH, chemistry
*Oligoribonucleotides: CS, chemical synthesis
Oligoribonucleotides: CH, chemistry
CAS REGISTRY NO.: 73120-97-5 (bis(3'-5')cyclic diuridine monophosphate)
CHEMICAL NAME: 0 (Dinucleoside Phosphates); 0 (Nucleotides, Cyclic); 0 (Oligoribonucleotides)

L94 ANSWER 17 OF 23 MEDLINE on STN
ACCESSION NUMBER: 94114114 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8286055
TITLE: Molecular structure of cyclic diguanylic acid at 1 A resolution of two crystal forms: self-association, interactions with metal ion/planar dyes and modeling studies.
AUTHOR: Guan Y; Gao Y G; Liaw Y C; Robinson H; Wang A H

CORPORATE SOURCE: Division of Biophysics, University of Illinois at Urbana-Champaign 61801.
CONTRACT NUMBER: CA-52506 (United States NCI)
GM-41612 (United States NIGMS)
SOURCE: Journal of biomolecular structure & dynamics, (1993 Oct) Vol. 11, No. 2, pp. 253-76.
Journal code: 8404176. ISSN: 0739-1102.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199402
ENTRY DATE: Entered STN: 12 Mar 1994
Last Updated on STN: 3 Feb 1997
Entered Medline: 22 Feb 1994

ABSTRACT:
Cyclic ribodiguanylic acid, c-(GpGp), is the endogenous effector regulator of cellulose synthase. Its three dimensional structure from two different crystal forms (tetragonal and trigonal) has been determined by x-ray diffraction analysis at 1 A resolution. Both structures were solved by direct methods and refined by block-matrix least squares refinement to R-factors of 0.112 (tetragonal) and 0.119 (trigonal). In both crystal forms, two independent c-(GpGp) molecules associate with each other to form a self-intercalated dimer. All four c-(GpGp) molecules have very similar backbone conformation. The riboses are in the C3'-endo pucker with pseudorotation angles ranging from -7.2 degrees to 16.5 degrees and the bases have anti glycosyl chi angles (-175.5 degrees to 179.7 degrees). In the tetragonal form, a hydrated cobalt ion is found to coordinate to two N7 atoms of adjacent guanines, forcing these two guanines to destack with a large dihedral angle (33 degrees). This metal coordination mechanism has been noted previously in other Pt- or Co-GMP complexes and may be relevant to the binding of the anticancer drug cisplatin to a GpG sequence in DNA. A model of the adduct between cisplatin and a d(CAATGGATTG) duplex has been constructed in which the induced bending of the DNA helix at the Pt crosslinking site is 33 degrees, consistent with earlier electrophoretic analyses. Moreover, c-(GpGp) exhibits unusual spectral properties not seen in other cyclic dinucleotides. It interacts with planar organic intercalator molecules in ways similar to double helical DNA. We propose a cage-like model consisting of a tetrameric c-(GpGp) aggregate in which a large cavity (host molecule) is generated to afford a binding site for certain planar intercalators (guests molecules). The aggregate likely uses a hydrogen bonding scheme the same as that found in the G-quartet molecules, e.g., telomere DNA. The conformation of c-(GpGp) also suggests that certain nearest-neighbor intercalators may be synthesized on the basis of its unique molecular framework. Modeling studies have been carried out to test this hypothesis.

CONTROLLED TERM: Base Sequence
Binding Sites
Cisplatin: CH, chemistry
Cobalt: CH, chemistry
Computer Simulation
Crystallography, X-Ray
*Cyclic GMP: AA, analogs & derivatives
Cyclic GMP: CH, chemistry
DNA: CH, chemistry
*DNA Adducts
Hydrogen Bonding
Models, Molecular
Molecular Sequence Data
*Nucleic Acid Conformation

Platinum: CH, chemistry
Spectrophotometry, Ultraviolet
CAS REGISTRY NO.: 15663-27-1 (Cisplatin); 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7440-06-4 (Platinum); 7440-48-4 (Cobalt); 7665-99-8 (Cyclic GMP); 9007-49-2 (DNA)
CHEMICAL NAME: 0 (DNA Adducts); 0 (cisplatin-DNA adduct)

L94 ANSWER 18 OF 23 MEDLINE on STN
ACCESSION NUMBER: 91271411 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1647035
TITLE: Polypeptide composition of bacterial cyclic diguanylic acid-dependent cellulose synthase and the occurrence of immunologically crossreacting proteins in higher plants.
AUTHOR: Mayer R; Ross P; Weinhouse H; Amikam D; Volman G; Ohana P; Calhoon R D; Wong H C; Emerick A W; Benziman M
CORPORATE SOURCE: Department of Biological Chemistry, Hebrew University of Jerusalem, Israel.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1991 Jun 15) Vol. 88, No. 12, pp. 5472-6.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199107
ENTRY DATE: Entered STN: 11 Aug 1991
Last Updated on STN: 11 Aug 1991
Entered Medline: 19 Jul 1991

ABSTRACT:
To comprehend the catalytic and regulatory mechanism of the cyclic diguanylic acid (c-di-GMP)-dependent cellulose synthase of Acetobacter xylinum and its relatedness to similar enzymes in other organisms, the structure of this enzyme was analyzed at the polypeptide level. The enzyme, purified 350-fold by enzyme-product entrapment, contains three major peptides (90, 67, and 54 kDa), which, based on direct photoaffinity and immunochemical labeling and amino acid sequence analysis, are constituents of the native cellulose synthase. Labeling of purified synthase with either [32P]c-di-GMP or [alpha-32P]UDP-glucose indicates that activator- and substrate-specific binding sites are most closely associated with the 67- and 54-kDa peptides, respectively, whereas marginal photolabeling is detected in the 90-kDa peptide. However, antibodies raised against a protein derived from the cellulose synthase structural gene (bcsB) specifically label all three peptides. Further, the N-terminal amino acid sequences determined for the 90- and 67-kDa peptides share a high degree of homology with the amino acid sequence deduced from the gene. We suggest that the structurally related 67- and 54-kDa peptides are fragments proteolytically derived from the 90-kDa peptide encoded by bcsB. The anti-cellulose synthase antibodies crossreact with a similar set of peptides derived from other cellulose-producing microorganisms and plants such as Agrobacterium tumefaciens, Rhizobium leguminosarum, mung bean, peas, barley, and cotton. The occurrence of such cellulose synthase-like structures in plant species suggests that a common enzymatic mechanism for cellulose biogenesis is employed throughout nature.
CONTROLLED TERM: Affinity Labels
Amino Acid Sequence
*Arabidopsis Proteins
Bacteria: EN, enzymology
Blotting, Western
Cross Reactions

*Cyclic GMP: AA, analogs & derivatives
Cyclic GMP: ME, metabolism
Electrophoresis, Polyacrylamide Gel
Enzyme Activation
*Glucosyltransferases: ME, metabolism
Molecular Sequence Data
*Peptides: AN, analysis
*Plants: ME, metabolism
Substrate Specificity
CAS REGISTRY NO.: 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7665-99-8 (Cyclic GMP)
CHEMICAL NAME: 0 (Affinity Labels); 0 (Arabidopsis Proteins); 0 (Peptides); EC 2.4.1.- (Glucosyltransferases); EC 2.4.1.- (PRC1 protein, Arabidopsis); EC 2.4.1.12 (cellulose synthase (UDP-forming))

L94 ANSWER 19 OF 23 MEDLINE on STN
ACCESSION NUMBER: 92361247 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1668373
TITLE: Evidence for a cyclic diguanylic acid-dependent cellulose synthase in plants.
AUTHOR: Amor Y; Mayer R; Benziman M; Delmer D
CORPORATE SOURCE: Department of Botany, Hebrew University of Jerusalem, Israel.
SOURCE: The Plant cell, {1991 Sep} Vol. 3, No. 9, pp. 989-95.
Journal code: 9208688. ISSN: 1040-4651.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199209
ENTRY DATE: Entered STN: 25 Sep 1992
Last Updated on STN: 25 Sep 1992
Entered Medline: 15 Sep 1992

ABSTRACT:
Because numerous attempts to detect an activity for a cellulose synthase in plants have failed, we have taken a different approach toward detecting polypeptides involved in this process. The uniqueness of the structure and function of cyclic diguanylic acid (c-di-GMP) as an activator of the cellulose synthase of the bacterium Acetobacter xylinum makes it an attractive probe to use in a search for a c-di-GMP receptor that might be involved in the process in plants. Direct photolabeling with 32P-c-di-GMP has been used, therefore, to identify in plants two membrane polypeptides of 83 and 48 kD derived from cotton fibers that possess properties consistent with their being components of a c-di-GMP-dependent cellulose synthase. Based upon several criteria, the 48-kD species is proposed to be derived by proteolytic cleavage of the 83-kD polypeptide. Both polypeptides bind c-di-GMP with high affinity and specificity and show antigenic relatedness to the bacterial cellulose synthase, and the N-terminal sequence of the 48-kD polypeptide also indicates relatedness to the bacterial synthase. Ability to detect both cotton fiber polypeptides by photolabeling increases markedly in extracts derived from fibers entering the active phase of secondary wall cellulose synthesis. These results provide a basis for future work aimed at identifying and characterizing genes involved in cellulose synthesis in plants.
CONTROLLED TERM: Acetobacter: EN, enzymology
Amino Acid Sequence
Cloning, Molecular

Cyclic GMP: AA, analogs & derivatives
Cyclic GMP: ME, metabolism
*Glucosyltransferases: AN, analysis
Glucosyltransferases: GE, genetics
*Gossypium: EN, enzymology
Gossypium: GE, genetics
Gossypium: GD, growth & development
*Membrane Proteins: AN, analysis
Membrane Proteins: GE, genetics
Membrane Proteins: IM, immunology
Membrane Proteins: ME, metabolism
*Plant Proteins: AN, analysis
Plant Proteins: GE, genetics
Plant Proteins: IM, immunology
Plant Proteins: ME, metabolism
Sequence Homology, Nucleic Acid
Substrate Specificity

CAS REGISTRY NO.: 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7665-99-8 (Cyclic GMP)

CHEMICAL NAME: 0 (Membrane Proteins); 0 (Plant Proteins); EC 2.4.1.- (Glucosyltransferases); EC 2.4.1.- (cellulose synthase (cyclic diguanylic acid))

L94 ANSWER 20 OF 23 MEDLINE on STN

ACCESSION NUMBER: 91035415 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 2172238

TITLE: The cyclic diguanylic acid regulatory system of cellulose synthesis in Acetobacter xylinum. Chemical synthesis and biological activity of cyclic nucleotide dimer, trimer, and phosphothioate derivatives.

AUTHOR: Ross P; Mayer R; Weinhouse H; Amikam D; Huggirat Y; Benziman M; de Vroom E; Fidder A; de Paus P; Sliedregt L A; +

CORPORATE SOURCE: Department of Biological Chemistry, Hebrew University of Jerusalem, Israel.

SOURCE: The Journal of biological chemistry, (1990 Nov 5) Vol. 265, No. 31, pp. 18933-43.
Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199012

ENTRY DATE: Entered STN: 8 Feb 1991
Last Updated on STN: 8 Feb 1991
Entered Medline: 10 Dec 1990

ABSTRACT:
An unusual compound, cyclic-bis(3'----5') diguanylic acid (c-di-GMP or cGpGp), is involved in the regulation of cellulose synthesis in the bacterium Acetobacter xylinum. This cyclic dinucleotide acts as an allosteric, positive effector of cellulose synthase activity in vitro (Ka = 0.31 microM) and is inactivated via degradation by a Ca2(+)-sensitive phosphodiesterase, PDE-A (Km = 0.25 microM). A series of 13 analogs cyclic dimer and trimer nucleotides were synthesized, employing a phosphotriester approach, and tested for the ability to mimick c-di-GMP as activators of cellulose synthase and as substrates for PDE-A. Seven of the synthetic compounds stimulate cellulose synthase activity and all of these activators undergo the Ca2(+)-inhibited degradation reaction. The order of affinities for synthase activators is cGpGp approximately cdGpGp approximately cGp(S)Gp (S-diastereomer) greater than cIpGp greater than cdGpdGp greater than cXpGp greater than cIpIp greater than

cGp(S)Gp (R-diastereomer). Three cyclic dinucleotides of negligible affinity for either enzyme are cApAp, cUpUp, and cCpCp. This same order of affinities essentially pertains to the analogs as inhibitors of PDE-A activity, but at least one cyclic dinucleotide, cXpXp, which does not bind to cellulose synthase, is also a substrate for the degradation reaction, demonstrating that although the two enzymes share a similar, high degree of specificity for c-di-GMP, their cyclic dinucleotide binding sites are not identical. Phosphodiester bonds of activators in which an exocyclic oxygen is replaced with an atom of sulfur (cGp(S)Gp isomers) resist the action of PDE-A, and such derivatives may be prototypes for synthetic non-hydrolyzable c-di-GMP analogs.

CONTROLLED TERM: Allosteric Regulation
*Arabidopsis Proteins
Calcium: PD, pharmacology
*Cellulose: BI, biosynthesis
*Cyclic GMP: AA, analogs & derivatives
Cyclic GMP: CS, chemical synthesis
Cyclic GMP: PD, pharmacology
*Gluconacetobacter xylinus: ME, metabolism
Glucosyltransferases: ME, metabolism
Indicators and Reagents
Structure-Activity Relationship
Uridine Diphosphate Glucose: ME, metabolism

CAS REGISTRY NO.: 133-89-1 (Uridine Diphosphate Glucose); 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7440-70-2 (Calcium); 7665-99-8 (Cyclic GMP); 9004-34-6 (Cellulose)

CHEMICAL NAME: 0 (Arabidopsis Proteins); 0 (Indicators and Reagents); EC 2.4.1.- (Glucosyltransferases); EC 2.4.1.- (PRC1 protein, Arabidopsis); EC 2.4.1.12 (cellulose synthase (UDP-forming))

L94 ANSWER 21 OF 23 MEDLINE on STN
ACCESSION NUMBER: 90222203 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2158107
TITLE: Atomic-resolution structure of the cellulose synthase regulator cyclic diguanylic acid.
AUTHOR: Egli M; Gessner R V; Williams L D; Quigley G J; van der Marel G A; van Boom J H; Rich A; Frederick C A
CORPORATE SOURCE: Department of Biology, Massachusetts Institute of Technology, Cambridge 02139.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1990 Apr) Vol. 87, No. 8, pp. 3235-9.
Journal code: 7505876. ISSN: 0027-8424.
Report No.: NASA-90222203.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199005
ENTRY DATE: Entered STN: 22 Jun 1990
Last Updated on STN: 22 Jun 1990
Entered Medline: 24 May 1990

ABSTRACT:
Cyclic diguanylic acid acts as a regulator for cellulose synthase activity in the bacterium Acetobacter xylinum. We report the x-ray crystal structure of the regulator at atomic resolution. The structure contains two independent molecules that adopt almost identical conformations. The two molecules form

self-intercalated units that are stacked on each other. Two different G.G base-pairing modes occur between the stacks. The more stable one has two or possibly three hydrogen bonds between two guanines and is related to the type of hydrogen bonding that is believed to exist between G-rich strands at the ends of chromosomes.

CONTROLLED TERM: Acetobacter: EN, enzymology
Base Composition
*Cyclic GMP: AA, analogs & derivatives
Glucosyltransferases: AI, antagonists & inhibitors
Hydrogen Bonding
Models, Molecular
Molecular Conformation
Molecular Structure
X-Ray Diffraction

CAS REGISTRY NO.: 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7665-99-8 (Cyclic GMP)

CHEMICAL NAME: EC 2.4.1.- (Glucosyltransferases); EC 2.4.1.29 (cellulose synthase (GDP-forming))

L94 ANSWER 22 OF 23 MEDLINE on STN

ACCESSION NUMBER: 90292211 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 2162785

TITLE: Cyclic diguanylic acid behaves as a host molecule for planar intercalators.

AUTHOR: Liaw Y C; Gao Y G; Robinson H; Sheldrick G M; Sliedregt L A; van der Marel G A; van Boom J H; Wang A H

CORPORATE SOURCE: Department of Physiology and Biophysics, University of Illinois, Urbana 61801.

SOURCE: FEBS letters, (1990 May 21) Vol. 264, No. 2, pp. 223-7.
Journal code: 0155157. ISSN: 0014-5793.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199007

ENTRY DATE: Entered STN: 7 Sep 1990
Last Updated on STN: 7 Sep 1990
Entered Medline: 31 Jul 1990

ABSTRACT:
Cyclic ribodiguanylic acid, c-(GpGp), is the endogenous effector regulator of cellulose synthase. Its three-dimensional structure from two different crystal forms (tetragonal and trigonal) has been determined by X-ray diffraction analysis at 1 A resolution. In both crystal forms, two independent c-(GpGp) molecules associate with each other to form a self-intercalated dimer. A hydrated cobalt ion is found to coordinate to two N7 atoms of adjacent guanines, forcing these two guanines to destack with a large dihedral angle (32 degrees), in the dimer of the tetragonal form. This metal coordination mechanism may be relevant to that of the anticancer drug cisplatin. Moreover, c-(GpGp) exhibits unusual spectral properties not seen in any other cyclic dinucleotide. It interacts with planar organic intercalator molecules in ways similar to double helical DNA. We propose a cage-like model consisting of a tetrameric c-(GpGp) aggregate in which a large cavity ('host') is generated to afford a binding site for certain planar intercalators ('guests').

CONTROLLED TERM: 5'-Guanylic Acid: AA, analogs & derivatives
*5'-Guanylic Acid: ME, metabolism
*Cyclic GMP: AA, analogs & derivatives

Cyclic GMP: ME, metabolism
*Guanine Nucleotides: ME, metabolism
*Intercalating Agents
Molecular Structure
Spectrophotometry, Ultraviolet
X-Ray Diffraction
CAS REGISTRY NO.: 17332-09-1 (GpGp); 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7665-99-8 (Cyclic GMP); 85-32-5 (5'-Guanylic Acid)
CHEMICAL NAME: 0 (Guanine Nucleotides); 0 (Intercalating Agents)

L94 ANSWER 23 OF 23 MEDLINE on STN
ACCESSION NUMBER: 90078110 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2556370
TITLE: Cyclic diguanylic acid and cellulose synthesis in Agrobacterium tumefaciens.
AUTHOR: Amikam D; Benziman M
CORPORATE SOURCE: Department of Biological Chemistry, Hebrew University of Jerusalem, Israel.
SOURCE: Journal of bacteriology, (1989 Dec) Vol. 171, No. 12, pp. 6649-55.
Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199001
ENTRY DATE: Entered STN: 28 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 25 Jan 1990
ABSTRACT:
The occurrence of the novel regulatory nucleotide bis(3',5')-cyclic diguanylic acid (c-di-GMP) and its relation to cellulose biogenesis in the plant pathogen Agrobacterium tumefaciens was studied. c-di-GMP was detected in acid extracts of 32P-labeled cells grown in various media, and an enzyme responsible for its formation from GTP was found to be present in cell-free preparations. Cellulose synthesis in vivo was quantitatively assessed with [14C]glucose as a tracer. The organism produced cellulose during growth in the absence of plant cells, and this capacity was retained in resting cells. Synthesis of a cellulosic product from UDP-glucose in vitro with membrane preparations was markedly stimulated by c-di-GMP and its precursor GTP and was further enhanced by Ca2+. The calcium effect was attributed to inhibition of a c-di-GMP-degrading enzyme shown to be present in the cellulose synthase-containing membranes.
CONTROLLED TERM: *Arabidopsis Proteins
*Cellulose: BI, biosynthesis
*Cyclic GMP: AA, analogs & derivatives
Cyclic GMP: ME, metabolism
Glucosyltransferases: ME, metabolism
Guanosine Triphosphate: ME, metabolism
Kinetics
Phosphorus Radioisotopes
Radioisotope Dilution Technique
Rhizobium: GD, growth & development
*Rhizobium: ME, metabolism
CAS REGISTRY NO.: 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7665-99-8 (Cyclic GMP); 86-01-1 (Guanosine Triphosphate); 9004-34-6 (Cellulose)
CHEMICAL NAME: 0 (Arabidopsis Proteins); 0 (Phosphorus Radioisotopes); EC 2.4.1.- (Glucosyltransferases); EC 2.4.1.- (PRC1 protein,

Arabidopsis); EC 2.4.1.12 (cellulose synthase
(UDP-forming))

=> fil reg; s 61093-23-0 or 73120-97-5
FILE 'REGISTRY' ENTERED AT 15:39:42 ON 19 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 18 MAR 2008 HIGHEST RN 1008796-87-9
DICTIONARY FILE UPDATES: 18 MAR 2008 HIGHEST RN 1008796-87-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

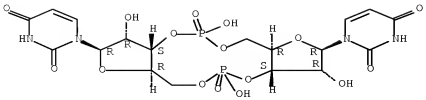
1 61093-23-0
(61093-23-0/RN)
1 73120-97-5
(73120-97-5/RN)
L95 2 61093-23-0 OR 73120-97-5

REGISTRY RECORDS FOR HIT RNs IN MEDLINE

=> d ide 1-2

L95 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2008 ACS on STN
RN 73120-97-5 REGISTRY
ED Entered STN: 16 Nov 1984
CN 3'-Uridylic acid, uridylyl-(3'→5')-, cyclic nucleotide (9CI) (CA
INDEX NAME)
OTHER CA INDEX NAMES:
CN 2H,7H-Difuro[3,2-d:3',2'-j][1,3,7,9,2,8]tetraoxadiphosphacyclododecin,
3'-uridylic acid deriv.
CN Uridine, 5'-O-phosphoryluridylyl-(3'→ 5')-, cyclic nucleotide (7CI)
FS STEREOSEARCH
MF C18 H22 N4 O16 P2
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, MEDLINE
(*File contains numerically searchable property data)

Absolute stereochemistry.



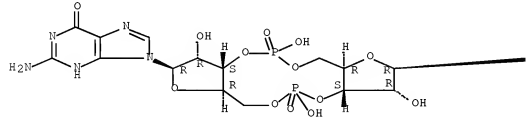
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8 REFERENCES IN FILE CA (1907 TO DATE)
8 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

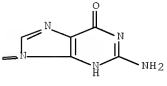
L95 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2008 ACS on STN
RN 61093-23-0 REGISTRY
ED Entered STN: 16 Nov 1984
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2H,7H-Difuro[3,2-d:3',2'-j][1,3,7,9,2,8]tetraoxadiphosphacyclododecin, 3'-guanylic acid deriv.
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic nucleotide
OTHER NAMES:
CN 3',5'-Cyclic diguanylic acid
FS STEREOSEARCH
DR 132182-17-3
MF C20 H24 N10 O14 P2
CI COM
LC STN Files: CA, CAPLUS, CASREACT, CHEMCATS, CSCHEM, MEDLINE, TOXCENTER, USPATFULL

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

92 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
92 REFERENCES IN FILE CAPLUS (1907 TO DATE)

TEXT SEARCH

```
=> fil medl agricola pascal caba wpix biotechno biosis esbio lifesci confsci
biotechds dissabs bioeng embase; d que 170; s 170 not 173; fil capl; d que 181; s
181 not 182,116,192
FILE 'MEDLINE' ENTERED AT 15:40:36 ON 19 MAR 2008

FILE 'AGRICOLA' ENTERED AT 15:40:36 ON 19 MAR 2008

FILE 'PASCAL' ENTERED AT 15:40:36 ON 19 MAR 2008
Any reproduction or dissemination in part or in full,
by means of any process and on any support whatsoever
is prohibited without the prior written agreement of INIST-CNRS.
COPYRIGHT (C) 2008 INIST-CNRS. All rights reserved.

FILE 'CABA' ENTERED AT 15:40:36 ON 19 MAR 2008
COPYRIGHT (C) 2008 CAB INTERNATIONAL (CABI)

FILE 'WPIX' ENTERED AT 15:40:36 ON 19 MAR 2008
COPYRIGHT (C) 2008 THE THOMSON CORPORATION

FILE 'BIOTECHNO' ENTERED AT 15:40:36 ON 19 MAR 2008
COPYRIGHT (C) 2008 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'BIOSIS' ENTERED AT 15:40:36 ON 19 MAR 2008
Copyright (c) 2008 The Thomson Corporation

FILE 'ESBIOBASE' ENTERED AT 15:40:36 ON 19 MAR 2008
COPYRIGHT (C) 2008 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'LIFESCI' ENTERED AT 15:40:36 ON 19 MAR 2008
COPYRIGHT (C) 2008 Cambridge Scientific Abstracts (CSA)

FILE 'CONFSCI' ENTERED AT 15:40:36 ON 19 MAR 2008
COPYRIGHT (C) 2008 Cambridge Scientific Abstracts (CSA)

FILE 'BIOTECHDS' ENTERED AT 15:40:36 ON 19 MAR 2008
COPYRIGHT (C) 2008 THE THOMSON CORPORATION

FILE 'DISSABS' ENTERED AT 15:40:36 ON 19 MAR 2008
COPYRIGHT (C) 2008 ProQuest Information and Learning Company; All Rights Reserved.

FILE 'BIOENG' ENTERED AT 15:40:36 ON 19 MAR 2008
COPYRIGHT (C) 2008 Cambridge Scientific Abstracts (CSA)

FILE 'EMBASE' ENTERED AT 15:40:36 ON 19 MAR 2008
Copyright (c) 2008 Elsevier B.V. All rights reserved.


L50         298 SEA CYCLIC(W) DI(W)((GUANOSINE(2W)(MONOPHOSPHATE OR MONO
                PHOSPHATE)) OR GMP)
L51         117 SEA CYCLIC(W)(DINUCLEOTIDE OR (DI NUCLEOTIDE))
L52       76606 SEA BIOFILM# OR BIO FILM#
L53      287453 SEA VIRULENCE
L54      304524 SEA COLONIZ? OR COLONIS?
L70         182 SEA (L50 OR L51) AND (L52 OR L53 OR L54)


L96         161 L70 NOT L73  L73=INVENTOR SEARCH ANSWER SET
```

```
FILE 'CAPLUS' ENTERED AT 15:40:42 ON 19 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 19 Mar 2008  VOL 148 ISS 12
FILE LAST UPDATED: 18 Mar 2008  (20080318/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE


L23         4983 SEA FILE=CAPLUS ABB=ON  COLONIZ?/OBI
L27        25812 SEA FILE=CAPLUS ABB=ON  VIRULENCE/CW
L28        13036 SEA FILE=CAPLUS ABB=ON  BIOFILM#/OBI
L74           41 SEA FILE=CAPLUS ABB=ON  CYCLIC/OBI(W) DI/OBI(W)((GUANOSINE/OBI(
                 2W)(MONOPHOSPHATE/OBI OR MONO PHOSPHATE/OBI)) OR GMP/OBI)
L75           28 SEA FILE=CAPLUS ABB=ON  CYCLIC/OBI(W)(DINUCLEOTIDE/OBI OR (DI
                 NUCLEOTIDE/OBI))
L78           18 SEA FILE=CAPLUS ABB=ON  (L74 OR L75) AND (L23 OR L27 OR L28)
L80           18 SEA FILE=CAPLUS ABB=ON  L74(W)PHOSPHODIESTERASE#/OBI
L81           10 SEA FILE=CAPLUS ABB=ON  L78 NOT L80



L97            9 L81 NOT (L82 OR L16 OR L92)   L82,L16,L92 WERE PREVIOUSLY DISPLAYED

=> dup rem l97,l96
FILE 'CAPLUS' ENTERED AT 15:40:49 ON 19 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'MEDLINE' ENTERED AT 15:40:49 ON 19 MAR 2008

FILE 'AGRICOLA' ENTERED AT 15:40:49 ON 19 MAR 2008

FILE 'PASCAL' ENTERED AT 15:40:49 ON 19 MAR 2008
Any reproduction or dissemination in part or in full,
by means of any process and on any support whatsoever
is prohibited without the prior written agreement of INIST-CNRS.
COPYRIGHT (C) 2008 INIST-CNRS. All rights reserved.

FILE 'CABA' ENTERED AT 15:40:49 ON 19 MAR 2008
```

```
COPYRIGHT (C) 2008 CAB INTERNATIONAL (CABI)

FILE 'WPIX' ENTERED AT 15:40:49 ON 19 MAR 2008
COPYRIGHT (C) 2008 THE THOMSON CORPORATION

FILE 'BIOSIS' ENTERED AT 15:40:49 ON 19 MAR 2008
Copyright (c) 2008 The Thomson Corporation

FILE 'ESBIOBASE' ENTERED AT 15:40:49 ON 19 MAR 2008
COPYRIGHT (C) 2008 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'LIFESCI' ENTERED AT 15:40:49 ON 19 MAR 2008
COPYRIGHT (C) 2008 Cambridge Scientific Abstracts (CSA)

FILE 'CONFSCI' ENTERED AT 15:40:49 ON 19 MAR 2008
COPYRIGHT (C) 2008 Cambridge Scientific Abstracts (CSA)

FILE 'BIOTECHDS' ENTERED AT 15:40:49 ON 19 MAR 2008
COPYRIGHT (C) 2008 THE THOMSON CORPORATION

FILE 'BIOENG' ENTERED AT 15:40:49 ON 19 MAR 2008
COPYRIGHT (C) 2008 Cambridge Scientific Abstracts (CSA)

FILE 'EMBASE' ENTERED AT 15:40:49 ON 19 MAR 2008
Copyright (c) 2008 Elsevier B.V. All rights reserved.
PROCESSING COMPLETED FOR L97
PROCESSING COMPLETED FOR L96
L98          39 DUP REM L97 L96 (131 DUPLICATES REMOVED)
                ANSWERS '1-9' FROM FILE CAPLUS
                ANSWERS '10-28' FROM FILE MEDLINE
                ANSWERS '29-30' FROM FILE PASCAL
                ANSWERS '31-32' FROM FILE BIOSIS
                ANSWERS '33-34' FROM FILE ESBIOBASE
                ANSWER '35' FROM FILE LIFESCI
                ANSWERS '36-37' FROM FILE CONFSCI
                ANSWER '38' FROM FILE BIOENG
                ANSWER '39' FROM FILE EMBASE

=> d ibib abs hitind 1-9; d iall 10-39

L98  ANSWER 1 OF 39  CAPLUS  COPYRIGHT 2008 ACS on STN DUPLICATE 8
ACCESSION NUMBER:         2006:383966  CAPLUS  Full-text
DOCUMENT NUMBER:          144:428461
TITLE:                    Methods for microbial biofilm destruction
                          and interference with microbial cellular physiology
INVENTOR(S):              Spormann, Alfred M.; Thormann, Kai M.; Saville, Renee
                          M.
PATENT ASSIGNEE(S):       The Board of Trustees of the Leland Stanford Junior
                          University, USA
SOURCE:                   PCT Int. Appl., 41 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ----------------    ----   --------    --------------------   --------
     WO 2006045041        A2    20060427    WO 2005-US37880        20051018
     WO 2006045041        A3    20070426
```

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2004-619973P P 20041018

OTHER SOURCE(S): MARPAT 144:428461

AB The formation and maintenance of microbial biofilms is shown to be dependent on signaling pathways mediated by cyclic di-GMP. In the absence of such signaling, microbes detach from a biofilm, and thereby become more readily treatable with conventional antibiotics. Chemical or biol. means that interfere with cyclic-di-GMP signaling induce biofilm dissoln., providing for a new class of antibiotics. In one embodiment of the invention, the biofilm inhibitor is an analog of cyclic-di-GMP, which competitively or non-competitively blocks signaling. In another embodiment of the invention, the biofilm inhibitor is a genetic sequence that interferes with cyclic-di-GMP synthesis or signaling.

CC 9-2 (Biochemical Methods)
Section cross-reference(s): 10

ST microbial biofilm destruction interference cellular cyclic diGMP signaling

IT Protein motifs
(GGDEF-like domain; methods for microbial biofilm destruction and interference with microbial cellular physiol.)

IT Protein motifs
(NVDEF; methods for microbial biofilm destruction and interference with microbial cellular physiol.)

IT Shewanella oneidensis
(biofilm; methods for microbial biofilm destruction and interference with microbial cellular physiol.)

IT Signal transduction, biological
(cyclic di-GMP; methods for microbial biofilm destruction and interference with microbial cellular physiol.)

IT Polysaccharides, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(exopolysaccharides, operon, S. oneidensis comprising; methods for microbial biofilm destruction and interference with microbial cellular physiol.)

IT Operon
(mdx; methods for microbial biofilm destruction and interference with microbial cellular physiol.)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mdxA; methods for microbial biofilm destruction and interference with microbial cellular physiol.)

IT Antibacterial agents
Biofilms (microbial)
Microorganism
(methods for microbial biofilm destruction and interference with microbial cellular physiol.)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(mxdB; methods for microbial biofilm destruction and interference with microbial cellular physiol.)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mxdC; methods for microbial biofilm destruction and interference with microbial cellular physiol.)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mxdD; methods for microbial biofilm destruction and interference with microbial cellular physiol.)
IT 61093-23-0 146316-82-7, Diguanylate cyclase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods for microbial biofilm destruction and interference with microbial cellular physiol.)
IT 884547-25-5
RL: PRP (Properties)
(unclaimed protein sequence; methods for microbial biofilm destruction and interference with microbial cellular physiol.)
IT 884547-26-6 884547-27-7 884547-28-8
RL: PRP (Properties)
(unclaimed sequence; methods for microbial biofilm destruction and interference with microbial cellular physiol.)

L98 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 11
ACCESSION NUMBER: 2006:1263183 CAPLUS Full-text
DOCUMENT NUMBER: 146:96738
TITLE: Diguanylate cyclases control magnesium-dependent motility of Vibrio fischeri
AUTHOR(S): O'Shea, Therese M.; Klein, Adam H.; Geszvain, Kati; Wolfe, Alan J.; Visick, Karen L.
CORPORATE SOURCE: Department of Microbiology and Immunology, Loyola University Chicago, Maywood, IL, 60153, USA
SOURCE: Journal of Bacteriology (2006), 188(23), 8196-8205
CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Flagellar biogenesis and hence motility of Vibrio fischeri depends upon the presence of magnesium. In the absence of magnesium, cells contain few or no flagella and are poorly motile or nonmotile. To dissect the mechanism by which this regulation occurs, the authors screened transposon insertion mutants for those that could migrate through soft agar medium lacking added magnesium. The authors identified mutants with insertions in two distinct genes, VF0989 and VFA0959, which the authors termed mifA and mifB, resp., for magnesium-dependent induction of flagellation. Each gene encodes a predicted membrane-associated protein with diguanylate cyclase activity. Consistent with that activity, introduction into V. fischeri of medium-copy plasmids carrying these genes inhibited motility. Furthermore, multicopy expression of mifA induced other phenotypes known to be correlated with diguanylate cyclase activity, including cellulose biosynthesis and biofilm formation. To directly test their function, the authors introduced the wild-type genes on high-copy plasmids into Escherichia coli. The authors assayed for the production of cyclic di-GMP using two-dimensional thin-layer chromatog. and found that strains carrying these plasmids produced a small but reproducible spot that migrated with an Rf value consistent with cyclic di-GMP that was not produced by strains carrying the vector control. Disruptions of mifA or mifB increased flagellin levels, while multicopy expression decreased them. Semiquant. reverse transcription-PCR expts. revealed no significant difference in the amount of flagellin transcripts produced in either the presence or absence of Mg2+ by either vector control or mifA-overexpressing cells, indicating that

the impact of magnesium and cyclic-di-GMP primarily acts following transcription. Finally, the authors present a model for the roles of magnesium and cyclic di-GMP in the control of motility of V. fischeri.

CC 10-6 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 3

IT Biofilms (microbial)
Cell migration
Transcription, genetic
Vibrio fischeri
(identification and characterization of two diguanylate cyclase genes, mifA and mifB, that control magnesium-dependent motility of Vibrio fischeri)

IT Simulation and Modeling
(model for roles of magnesium and cyclic di-GMP in control of motility of V. fischeri)

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L98 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 14

ACCESSION NUMBER: 2006:302504 CAPLUS Full-text
DOCUMENT NUMBER: 144:484363
TITLE: Control of formation and cellular detachment from Shewanella oneidensis MR-1 biofilms by cyclic di-GMP
AUTHOR(S): Thormann, Kai M.; Duttler, Stefanie; Saville, Renee M.; Hyodo, Mamoru; Shukla, Soni; Hayakawa, Yoshihiro; Spormann, Alfred M.
CORPORATE SOURCE: Departments of Civil and Environmental Engineering, Stanford University, Stanford, CA, 94305-5429, USA
SOURCE: Journal of Bacteriology (2006), 188(7), 2681-2691
CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Stability and resilience against environmental perturbations are critical properties of medical and environmental biofilms and pose important targets for their control. Biofilm stability is determined by two mutually exclusive processes: attachment of cells to and detachment from the biofilm matrix. Using Shewanella oneidensis MR-1, an environmentally versatile, Fe(III) and Mn(IV) mineral-reducing microorganism, we identified mxdABCD as a new set of genes essential for formation of a three-dimensional biofilm. Mol. anal. revealed that mxdA encodes a cyclic bis(3',5')guanylic acid (cyclic di-GMP)-forming enzyme with an unusual GGDEF motif, i.e., NVDEF, which is essential for its function. MxdB encodes a putative membrane-associated glycosyl transferase. Both genes are essential for matrix attachment. The attachment-deficient phenotype of a ΔmxdA mutant was rescued by ectopic expression of VCA0956, encoding another diguanylate cyclase. Interestingly, a rapid cellular detachment from the biofilm occurred upon induction of yhjH, a gene encoding an enzyme that has been shown to have phosphodiesterase activity. In this way, it was possible to bypass the previously identified sudden depletion of mol. oxygen as an environmental trigger to induce biofilm dissoln. We propose a model for cyclic-di-GMP as a key intracellular regulator for controlling biofilm stability by shifting the state of a biofilm cell between attachment and detachment in a concentration-dependent manner.

CC 10-2 (Microbial, Algal, and Fungal Biochemistry)

ST Shewanella biofilm adsorption detachment cyclic diguanylate

IT Shewanella oneidensis
(MR-1; control of formation and cellular detachment from Shewanella oneidensis MR-1 biofilms by cyclic di-GMP)

IT Adhesion, biological
Biofilms (microbial)
Signal transduction, biological
(control of formation and cellular detachment from Shewanella oneidensis MR-1 biofilms by cyclic di-GMP)
IT Polysaccharides, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(exopolysaccharides, biosynthesis; control of formation and cellular detachment from Shewanella oneidensis MR-1 biofilms by cyclic di-GMP)
IT Operon
(mxdABCD, role in biofilm formation; control of formation and cellular detachment from Shewanella oneidensis MR-1 biofilms by cyclic di-GMP)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(yhjH; control of formation and cellular detachment from Shewanella oneidensis MR-1 biofilms by cyclic di-GMP)
IT 146316-82-7, Diguanylate cyclase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MxdA; control of formation and cellular detachment from Shewanella oneidensis MR-1 biofilms by cyclic di-GMP)
IT 9033-07-2, Glycosyltransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MxdB; control of formation and cellular detachment from Shewanella oneidensis MR-1 biofilms by cyclic di-GMP)
IT 338732-46-0, Cyclic diguanylate phosphodiesterase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(YhjH; control of formation and cellular detachment from Shewanella oneidensis MR-1 biofilms by cyclic di-GMP)
IT 61093-23-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(regulatory role in biofilm stability; control of formation and cellular detachment from Shewanella oneidensis MR-1 biofilms by cyclic di-GMP)
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L98 ANSWER 4 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 16
ACCESSION NUMBER: 2006:1280137 CAPLUS Full-text
DOCUMENT NUMBER: 147:5044
TITLE: The HD-GYP domain, cyclic Di-GMP signaling, and bacterial virulence to plants
AUTHOR(S): Dow, J. Maxwell; Fouhy, Yvonne; Lucey, Jean F.; Ryan, Robert P.
CORPORATE SOURCE: BIOMERIT Research Centre, Department of Microbiology, BioSciences Institute, National University of Ireland, Cork, Ire.
SOURCE: Molecular Plant-Microbe Interactions (2006), 19(12), 1378-1384
CODEN: MPMIEL; ISSN: 0894-0282
PUBLISHER: APS Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Cyclic di-GMP is an almost ubiquitous second messenger in bacteria that was first described as an allosteric activator of cellulose synthase but is now known to regulate a range of functions, including virulence in human and animal pathogens. Two protein domains, GGDEF and EAL, are implicated in the synthesis and degradation, resp., of cyclic di-GMP. These domains are widely distributed in bacteria, including plant pathogens. The majority of proteins with GGDEF and EAL domains contain addnl. signal input domains, suggesting that their activities are responsive to environmental cues. Recent studies have demonstrated that a third domain, HD-GYP, is also active in cyclic di-GMP degradation In the plant pathogen Xanthomonas campestris pv. campestris, a two-component signal transduction system comprising the HD-GYP domain regulatory protein RpfG and cognate sensor RpfC pos. controls virulence. The signals recognized by RpfC may include the cell-cell signal DSF, which also acts to regulate virulence in X. campestris pv. campestris. Here, the authors review these recent advances in our understanding of cyclic di-GMP signaling with particular reference to one or more roles in the bacterial pathogenesis of plants.

CC 10-0 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 11

IT Embryophyta
Eubacteria
Plants
Signal transduction, biological
Virulence (microbial)
(HD-GYP domain, cyclic Di-GMP signaling and bacterial virulence to plants)

IT Protein motifs
(HD-GYP; HD-GYP domain, cyclic Di-GMP signaling and bacterial virulence to plants)

IT 61093-23-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HD-GYP domain, cyclic Di-GMP signaling and bacterial virulence to plants)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L98 ANSWER 5 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 18

ACCESSION NUMBER: 2006:1289099 CAPLUS Full-text
DOCUMENT NUMBER: 146:138496
TITLE: Cyclic-di-GMP-mediated signalling within the σS network of Escherichia coli
AUTHOR(S): Weber, Harald; Pesavento, Christina; Possling, Alexandra; Tischendorf, Gilbert; Hengge, Regine
CORPORATE SOURCE: Institut fuer Biologie, Mikrobiologie, Freie Universitaet Berlin, Berlin, 14195, Germany
SOURCE: Molecular Microbiology (2006), 62(4), 1014-1034
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bis-(3'-5')-cyclic-di-guanosine monophosphate (c-di-GMP) is a bacterial signaling mol. produced by diguanylate cyclases (DGC, carrying GGDEF domains) and degraded by specific phosphodiesterases (PDE, carrying EAL domains). Neither its full physiol. impact nor its effector mechanisms are currently understood. Also, the existence of multiple GGDEF/EAL genes in the genomes of most species raises questions about output specificity and robustness of c-di-GMP signaling. Using microarray and gene fusion analyses, we demonstrate that at least five of the 29 GGDEF/EAL genes in Escherichia coli are not only stationary phase-induced under the control of the general stress response

master regulator σS (RpoS), but also exhibit differential control by addnl. environmental and temporal signals. Two of the corresponding proteins, YdaM (GGDEF only) and YciR (GGDEF + EAL), which in vitro show DGC and PDE activity, resp., play an antagonistic role in the expression of the biofilm-associated curli fimbriae. This control occurs at the level of transcription of the curli and cellulose regulator CsgD. Moreover, we show that H-NS pos. affects curli expression by inversely controlling the expression of ydaM and yciR. Furthermore, we demonstrate a temporally fine-tuned GGDEF cascade in which YdaM controls the expression of another GGDEF protein, YaiC. By genome-wide microarray anal., evidence is provided that YdaM and YciR strongly and nearly exclusively control CsgD-regulated genes. We conclude that specific GGDEF/EAL proteins have very distinct expression patterns, and when present in physiol. amts., can act in a highly precise, non-global and perhaps microcompartmented manner on a few or even a single specific target(s).

CC 10-2 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 3

ST cyclic diguanylate signal sigS transcription factor Escherichia stress temp; cdiGMP YdaM diguanylate cyclase YciR cyclic diguanylate phosphodiesterase Escherichia; CsgD gene transcription regulation YdaM YciR HNS protein Escherichia; gene expression microarray yaiC transcription regulation YdaM Escherichia growth; Escherichia biofilm virulence fimbriae YdaM YciR

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CsgD; σS-dependent proteins YdaM and YciR inversely control curli biosynthesis during biofilm formation by affecting transcription of regulator CsgD related to action of H-NS protein)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(H-NS; σS-dependent proteins YdaM and YciR inversely control curli biosynthesis during biofilm formation by affecting transcription of regulator CsgD related to action of H-NS protein)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(csgD; σS-dependent proteins YdaM and YciR inversely control curli biosynthesis during biofilm formation by affecting transcription of regulator CsgD related to action of H-NS protein)

IT DNA microarray technology
Escherichia coli
Signal transduction, biological
Stress, microbial
Temperature effects, biological
(cyclic-di-GMP-mediated signalling within σS network of Escherichia coli studied using DNA microarray anal. under stress conditions)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(rpoS; cyclic-di-GMP-mediated signalling within σS network of Escherichia coli studied using DNA microarray anal. under stress conditions)

IT Growth, microbial
(stationary phase; cyclic-di-GMP-mediated signalling within σS network of Escherichia coli studied using DNA microarray anal. under stress conditions)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(yaiC, regulation by YdaM; σS-dependent proteins YdaM and YciR inversely control curli biosynthesis during biofilm formation by affecting transcription of regulator CsgD related to action of H-NS

protein)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ycgG; cyclic-di-GMP-mediated signalling
within σS network of Escherichia coli studied using DNA
microarray anal. under stress conditions)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(yciR; cyclic-di-GMP-mediated signalling
within σS network of Escherichia coli studied using DNA
microarray anal. under stress conditions)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ydaM; cyclic-di-GMP-mediated signalling
within σS network of Escherichia coli studied using DNA
microarray anal. under stress conditions)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(yddV; cyclic-di-GMP-mediated signalling
within σS network of Escherichia coli studied using DNA
microarray anal. under stress conditions)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ydiV; cyclic-di-GMP-mediated signalling
within σS network of Escherichia coli studied using DNA
microarray anal. under stress conditions)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(yeaI; cyclic-di-GMP-mediated signalling
within σS network of Escherichia coli studied using DNA
microarray anal. under stress conditions)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(yedQ; cyclic-di-GMP-mediated signalling
within σS network of Escherichia coli studied using DNA
microarray anal. under stress conditions)
IT Biofilms (microbial)
Pilus
(σS-dependent proteins YdaM and YciR inversely control curli
biosynthesis during biofilm formation by affecting
transcription of regulator CsgD)
IT Transcriptional regulation
Virulence (microbial)
(σS-dependent proteins YdaM and YciR inversely control curli
biosynthesis during biofilm formation by affecting
transcription of regulator CsgD related to action of H-NS protein)
IT 338732-46-0, Cyclic diguanylate phosphodiesterase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(YciR; σS-dependent proteins YdaM and YciR inversely control
curli biosynthesis during biofilm formation by affecting
transcription of regulator CsgD)
IT 146316-82-7, Diguanylate cyclase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(YdaM and YaiC; σS-dependent proteins YdaM and YciR inversely
control curli biosynthesis during biofilm formation by
affecting transcription of regulator CsgD)
IT 61093-23-0, 3',5'-Cyclic diguanylic acid
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(cyclic-di-GMP-mediated signalling within σS network of Escherichia coli studied using DNA microarray anal. under stress conditions)
REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L98 ANSWER 6 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 19
ACCESSION NUMBER: 2006:1267114 CAPLUS Full-text
DOCUMENT NUMBER: 146:397889
TITLE: Cell-cell signaling, cyclic di-GMP turnover and regulation of virulence in Xanthomonas campestris
AUTHOR(S): Fouhy, Yvonne; Lucey, Jean F.; Ryan, Robert P.; Dow, J. Maxwell
CORPORATE SOURCE: BIOMERIT Research Centre, Department of Microbiology, BioSciences Institute, National University of Ireland, Cork, Ire.
SOURCE: Research in Microbiology (2006), 157(10), 899-904
CODEN: RMCREW; ISSN: 0923-2508
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The synthesis of virulence factors in the plant pathogen Xanthomonas campestris pathovar campestris is regulated by cell-cell signaling mediated by a diffusible signal factor (DSF), and by the RpfC/RpfG two-component regulatory system. Recent findings have indicated that the perception of the DSF signal requires the RpfC sensor and is linked to the degradation of the intracellular second messenger cyclic di-GMP by the HD-GYP domain regulator RpfG.
CC 10-0 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 11
IT Signal transduction, biological
Virulence (microbial)
Xanthomonas campestris campestris
(cell-cell signaling, cyclic di-GMP turnover and regulation of virulence in Xanthomonas campestris)
IT 7665-99-8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cell-cell signaling, cyclic di-GMP turnover and regulation of virulence in Xanthomonas campestris)
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L98 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 20
ACCESSION NUMBER: 2007:7773 CAPLUS Full-text
DOCUMENT NUMBER: 146:77652
TITLE: Mechanisms of cyclic-di-GMP signaling in bacteria
AUTHOR(S): Jenal, Urs; Malone, Jacob
CORPORATE SOURCE: Biozentrum of the University of Basel, Basel, CH-4056, Switz.
SOURCE: Annual Review of Genetics (2006), 40, 385-407
CODEN: ARVGB7; ISSN: 0066-4197
PUBLISHER: Annual Reviews Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Cyclic-di-GMP is a ubiquitous second messenger in bacteria. The recent discovery that c-di-GMP antagonistically controls motility and virulence of single, planktonic cells on one hand and cell adhesion and persistence of multicellular communities on the other has spurred interest in

this regulatory compound Cellular levels of c-di-GMP are controlled through the opposing activities of diguanylate cyclases and phosphodiesterases, which represent 2 large families of output domains found in bacterial one- and 2-component systems. This review concs. on structural and functional aspects of diguanylate cyclases and phosphodiesterases, and on their role in transmitting environmental stimuli into a range of different cellular functions. In addition, the authors examine several well-established model systems for c-di-GMP signaling, including Pseudomonas, Vibrio, Caulobacter, and Salmonella.

CC 10-0 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 6

IT Eubacteria
Second messenger system
Signal transduction, biological
Virulence (microbial)
(mechanisms of cyclic-di-GMP signaling in bacteria)

IT 9068-52-4, Cyclic GMP phosphodiesterase 61093-23-0, 3',5'-Cyclic diguanylic acid 146316-82-7, Diguanylate cyclase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mechanisms of cyclic-di-GMP signaling in bacteria)

REFERENCE COUNT: 120 THERE ARE 120 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L98 ANSWER 8 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 21

ACCESSION NUMBER: 2006:312378 CAPLUS Full-text
DOCUMENT NUMBER: 145:501953
TITLE: Cyclic di-GMP as a second messenger
AUTHOR(S): Roemling, Ute; Amikam, Dorit
CORPORATE SOURCE: Microbiology and Tumor Biology Center, Karolinska Institutet, Stockholm, SE-171 77, Swed.
SOURCE: Current Opinion in Microbiology (2006), 9(2), 218-228
CODEN: COMIF7; ISSN: 1369-5274
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. In many bacteria bis-(3',5')-cyclic dimeric guanosine monophosphate (c-di-GMP) signaling dets. the timing and amplitude of complex biol. processes from biofilm formation and virulence to photosynthesis. Thereby, the tightly regulated temporal and spatial activity patterns of GGDEF and EAL domain proteins, which synthesize and degrade c-di-GMP, resp., are currently being resolved. Although details of the mechanisms of c-di-GMP signaling are not yet determined, the recent presentation of PilZ as a candidate c-di-GMP binding-domain opens the field for exptl. investigations. Besides its role as an intracellular signaling mol. in bacteria, c-di-GMP also acts as an intercellular signaling mol. between prokaryotes and also has effects in eukaryotes that could provide a perspective in cancer treatment.

CC 10-0 (Microbial, Algal, and Fungal Biochemistry)

IT Biofilms (microbial)
Photosynthesis, biological
Second messenger system
Virulence (microbial)
(cyclic di-GMP as a second messenger)

IT 7665-99-8, Cyclic GMP
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cyclic di-GMP as a second messenger)

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L98 ANSWER 9 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1058301 CAPLUS Full-text
DOCUMENT NUMBER: 148:116340
TITLE: Cyclic di-GMP as an intracellular signal regulating bacterial biofilm formation
AUTHOR(S): Dow, John M.; Fouhy, Yvonne; Lucey, Jean.; Ryan, Robert P.
CORPORATE SOURCE: BIOMERIT Research Centre Department of Microbiology, (University College Cork), National University of Ireland Cork, Cork, Ire.
SOURCE: Biofilm Mode of Life (2007), 71-93. Editor(s): Kjelleberg, Staffan; Givskov, Michael. Horizon Bioscience: Wymondham, UK.
CODEN: 69JUXT; ISBN: 978-1-904933-33-5
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review. Cyclic di-GMP is a novel second messenger in bacteria that was first described as an allosteric activator of cellulose synthase in Gluconacetobacter xylinus. It is now established that this nucleotide regulates a range of functions including developmental transitions, aggregative behavior, adhesion, biofilm formation and virulence in diverse bacteria. The level of cyclic di-GMP in bacterial cells is influenced by both synthesis and degradation The GGDEF protein domain synthesizes cyclic di-GMP, whereas EAL and HD-GYP domains are involved in cyclic di-GMP hydrolysis. Bacterial genomes encode a number of proteins with GGDEF, EAL and HD-GYP domains. The majority of these proteins contain addnl. signal input domains, suggesting that their activities are responsive to environmental cues. An emerging theme is that high cellular levels of cyclic di-GMP promote biofilm formation and aggregative behavior whereas low cellular levels promote motility. The mechanism(s) by which cyclic di-GMP exerts its effects on these cellular functions is however poorly understood.
CC 10-0 (Microbial, Algal, and Fungal Biochemistry)
ST review bacteria biofilm intracellular signal cyclic di guanosine monophosphate
IT Biofilms (microbial)
Signal transduction, biological
(cyclic di-GMP as an intracellular signal regulating bacterial biofilm formation)
IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cyclic di-GMP; cyclic di-GMP as an intracellular signal regulating bacterial biofilm formation)
REFERENCE COUNT: 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L98 ANSWER 10 OF 39 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2008128123 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 18268318
TITLE: A cell-cell signaling sensor is required for virulence and insect transmission of Xylella fastidiosa.
AUTHOR: Chatterjee Subhadeep; Wistrom Christina; Lindow Steven E
CORPORATE SOURCE: Departments of Plant and Microbial Biology and Environmental Science, Policy, and Management, University

of California, Berkeley, CA 94720, USA.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2008 Feb 19) Vol. 105, No. 7, pp. 2670-5. Electronic Publication: 2008-02-11. Journal code: 7505876. E-ISSN: 1091-6490.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200803
ENTRY DATE: Entered STN: 22 Feb 2008
Last Updated on STN: 14 Mar 2008
Entered Medline: 13 Mar 2008

ABSTRACT:
Cell-cell signaling in Xylella fastidiosa, a xylem-colonizing plant pathogenic bacterium, mediated by a fatty acid Diffusible Signaling Factor (DSF), is required to colonize insect vectors and to suppress ***virulence*** to grape. Here, we show that a hybrid two-component regulatory protein RpfC is involved in negative regulation of DSF synthesis by RpfF in X. fastidiosa. X. fastidiosa rpfC mutants hyperexpress rpfF and overproduce DSF and are deficient in virulence and movement in the xylem vessels of grape. The expression of the genes encoding the adhesins FimA, HxfA, and HxfB is much higher in rpfC mutants, which also exhibit a hyperattachment phenotype in culture that is associated with their inability to migrate in xylem vessels and cause disease. rpfF mutants deficient in DSF production have the opposite phenotypes for all of these traits. RpfC is also involved in the regulation of other signaling components including rpfG, rpfB, a GGDEF domain protein that may be involved in intracellular signaling by modulating the levels of cyclic-di-GMP, and the ***virulence*** factors tolC and pglA required for disease. rpfC mutants are able to colonize the mouthparts of insect vectors and wild-type strains but are not transmitted as efficiently to new host plants, apparently because of their high levels of adhesiveness. Because of the conflicting contributions of adhesiveness and other traits to movement within plants and vectoring to new host plants, X. fastidiosa apparently coordinates these traits in a population-size-dependent fashion involving accumulation of DSF.

CONTROLLED TERM:
Adhesins, Bacterial: ME, metabolism
Animals
Bacterial Proteins: ME, metabolism
*Cell Communication
Gene Expression Regulation, Bacterial
*Insect Vectors: MI, microbiology
*Insects
Mutation: GE, genetics
Phenotype
*Plant Diseases: MI, microbiology
*Signal Transduction
Virulence
Xylella: ME, metabolism
*Xylella: PY, pathogenicity

CHEMICAL NAME: 0 (Adhesins, Bacterial); 0 (Bacterial Proteins)

L98 ANSWER 11 OF 39 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2007652249 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17586641
TITLE: BifA, a cyclic-Di-GMP phosphodiesterase, inversely regulates biofilm formation and swarming motility by Pseudomonas aeruginosa PA14.

AUTHOR: Kuchma Sherry L; Brothers Kimberly M; Merritt Judith H; Liberati Nicole T; Ausubel Frederick M; O'Toole George A
CORPORATE SOURCE: Department of Microbiology and Immunology, Dartmouth Medical School, Rm. 505, Vail Building, North College St., Hanover, NH 03755, USA.
CONTRACT NUMBER: 1-P20-RR01878 (United States NCRR)
AI51360 (United States NIAID)
SOURCE: Journal of bacteriology, (2007 Nov) Vol. 189, No. 22, pp. 8165-78. Electronic Publication: 2007-06-22.
Journal code: 2985120R. E-ISSN: 1098-5530.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200801
ENTRY DATE: Entered STN: 6 Nov 2007
Last Updated on STN: 15 Jan 2008
Entered Medline: 14 Jan 2008

ABSTRACT:
The intracellular signaling molecule, cyclic-di-GMP (c-di-GMP), has been shown to influence bacterial behaviors, including motility and biofilm formation. We report the identification and characterization of PA4367, a gene involved in regulating surface-associated behaviors in Pseudomonas aeruginosa. The PA4367 gene encodes a protein with an EAL domain, associated with c-di-GMP phosphodiesterase activity, as well as a GGDEF domain, which is associated with a c-di-GMP-synthesizing diguanylate cyclase activity. Deletion of the PA4367 gene results in a severe defect in swarming motility and a hyperbiofilm phenotype; thus, we designate this gene bifA, for biofilm formation. We show that BifA localizes to the inner membrane and, in biochemical studies, that purified BifA protein exhibits phosphodiesterase activity in vitro but no detectable diguanylate cyclase activity. Furthermore, mutational analyses of the conserved EAL and GGDEF residues of BifA suggest that both domains are important for the observed phosphodiesterase activity. Consistent with these data, the DeltabifA mutant exhibits increased cellular pools of c-di-GMP relative to the wild type and increased synthesis of a polysaccharide produced by the pel locus. This increased polysaccharide production is required for the enhanced ***biofilm*** formed by the DeltabifA mutant but does not contribute to the observed swarming defect. The DeltabifA mutation also results in decreased flagellar reversals. Based on epistasis studies with the previously described sadB gene, we propose that BifA functions upstream of SadB in the control of ***biofilm*** formation and swarming.

CONTROLLED TERM: Bacterial Proteins: GE, genetics
Bacterial Proteins: ME, metabolism
*Biofilms: GD, growth & development
Cell Membrane
*Cyclic GMP: AA, analogs & derivatives
Cyclic GMP: ME, metabolism
Gene Expression Regulation, Bacterial
Movement
Phosphoric Diester Hydrolases: GE, genetics
*Phosphoric Diester Hydrolases: ME, metabolism
Protein Transport
*Pseudomonas aeruginosa: CY, cytology
*Pseudomonas aeruginosa: EN, enzymology
CAS REGISTRY NO.: 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7665-99-8 (Cyclic GMP)

CHEMICAL NAME: 0 (Bacterial Proteins); EC 3.1.4.- (Phosphoric Diester Hydrolases)

L98 ANSWER 12 OF 39 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2007652250 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17586642
TITLE: SadC reciprocally influences biofilm formation and swarming motility via modulation of exopolysaccharide production and flagellar function.
AUTHOR: Merritt Judith H; Brothers Kimberly M; Kuchma Sherry L; O'Toole George A
CORPORATE SOURCE: Department of Microbiology and Immunology, Rm. 505, Vail Building, Dartmouth Medical School, Hanover, NH 03755, USA.
CONTRACT NUMBER: AI51360 (United States NIAID)
P20-RR018787 (United States NCRR)
T32 GM08704 (United States NIGMS)
SOURCE: Journal of bacteriology, (2007 Nov) Vol. 189, No. 22, pp. 8154-64. Electronic Publication: 2007-06-22.
Journal code: 2985120R. E-ISSN: 1098-5530.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200801
ENTRY DATE: Entered STN: 6 Nov 2007
Last Updated on STN: 15 Jan 2008
Entered Medline: 14 Jan 2008

ABSTRACT:
Pseudomonas aeruginosa has served as an important organism in the study of ***biofilm*** formation; however, we still lack an understanding of the mechanisms by which this microbe transitions to a surface lifestyle. A recent study of the early stages of biofilm formation implicated the control of flagellar reversals and production of an exopolysaccharide (EPS) as factors in the establishment of a stable association with the substratum and swarming motility. Here we present evidence that SadC (PA4332), an inner membrane-localized diguanylate cyclase, plays a role in controlling these cellular functions. Deletion of the sadC gene results in a strain that is defective in biofilm formation and a hyperswarmer, while multicopy expression of this gene promotes sessility. A DeltasadC mutant was additionally found to be deficient in EPS production and display altered reversal behavior while swimming in high-viscosity medium, two behaviors proposed to influence biofilm formation and swarming motility. Epistasis analysis suggests that the sadC gene is part of a genetic pathway that allows for the concomitant regulation of these aspects of P. aeruginosa surface behavior. We propose that SadC and the phosphodiesterase BifA (S. L. Kuchma et al., J. Bacteriol. 189:8165-8178, 2007), via modulating levels of the signaling molecule cyclic-di-GMP, coregulate swarming motility and biofilm formation as P. aeruginosa transitions from a planktonic to a surface-associated lifestyle.

CONTROLLED TERM: Bacterial Proteins: GE, genetics
Bacterial Proteins: ME, metabolism
*Biofilms: GD, growth & development
Congo Red
*Flagella: PH, physiology
Gene Expression Regulation, Bacterial
Movement
Mutation
*Polysaccharides, Bacterial: BI, biosynthesis
*Pseudomonas aeruginosa: CY, cytology

Pseudomonas aeruginosa: GE, genetics
*Pseudomonas aeruginosa: ME, metabolism
RNA, Messenger
Staining and Labeling
CAS REGISTRY NO.: 128531-82-8 (exopolysaccharide, Pseudomonas); 573-58-0 (Congo Red)
CHEMICAL NAME: 0 (Bacterial Proteins); 0 (Polysaccharides, Bacterial); 0 (RNA, Messenger)

L98 ANSWER 13 OF 39 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2007295150 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17400744
TITLE: ScrG, a GGDEF-EAL protein, participates in regulating swarming and sticking in Vibrio parahaemolyticus.
AUTHOR: Kim Yun-Kyeong; McCarter Linda L
CORPORATE SOURCE: Microbiology Department, The University of Iowa, Iowa City, IA 52242, USA.
SOURCE: Journal of bacteriology, (2007 Jun) Vol. 189, No. 11, pp. 4094-107. Electronic Publication: 2007-03-30.
Journal code: 2985120R. ISSN: 0021-9193.
COMMENT: Comment in: J Bacteriol. 2008 Feb;190(3):781-3. PubMed ID: 18065536
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200709
ENTRY DATE: Entered STN: 18 May 2007
Last Updated on STN: 7 Sep 2007
Entered Medline: 6 Sep 2007

ABSTRACT:
In this work, we describe a new gene controlling lateral flagellar gene expression. The gene encodes ScrG, a protein containing GGDEF and EAL domains. This is the second GGDEF-EAL-encoding locus determined to be involved in the regulation of swarming: the first was previously characterized and named scrABC (for "swarming and capsular polysaccharide regulation"). GGDEF and EAL domain-containing proteins participate in the synthesis and degradation of the nucleotide signal cyclic di-GMP (c-di-GMP) in many bacteria. Overexpression of scrG was sufficient to induce lateral flagellar gene expression in liquid, decrease biofilm formation, decrease cps gene expression, and suppress the DeltascrABC phenotype. Removal of its EAL domain reversed ScrG activity, converting ScrG to an inhibitor of swarming and activator of cps expression. Overexpression of scrG decreased the intensity of a (32)P-labeled nucleotide spot comigrating with c-di-GMP standard, whereas overexpression of scrG(Delta)(EAL) enhanced the intensity of the spot. Mutants with defects in scrG showed altered swarming and lateral flagellin production and colony morphology (but not swimming motility); furthermore, mutation of two GGDEF-EAL-encoding loci (scrG and scrABC) produced cumulative effects on swarming, lateral flagellar gene expression, lateral flagellin production and colony morphology. Mutant analysis supports the assignment of the primary in vivo activity of ScrG to acting as a phosphodiesterase. The data are consistent with a model in which multiple GGDEF-EAL proteins can influence the cellular nucleotide pool: a low concentration of c-di-GMP favors surface mobility, whereas high levels of this nucleotide promote a more adhesive Vibrio parahaemolyticus cell type.
CONTROLLED TERM: Amino Acid Sequence
Bacterial Adhesion: GE, genetics
*Bacterial Adhesion: PH, physiology
Bacterial Proteins: GE, genetics

Bacterial Proteins: ME, metabolism
*Bacterial Proteins: PH, physiology
Biofilms
Cyclic GMP: AA, analogs & derivatives
Flagella: GE, genetics
Flagella: ME, metabolism
Flagella: PH, physiology
Gene Deletion
Gene Expression Regulation, Bacterial
Immunoblotting
Models, Genetic
Molecular Sequence Data
Mutation
Phenotype
Sequence Homology, Amino Acid
Vibrio parahaemolyticus: GE, genetics
Vibrio parahaemolyticus: ME, metabolism
*Vibrio parahaemolyticus: PH, physiology
beta-Galactosidase: GE, genetics
beta-Galactosidase: ME, metabolism

CAS REGISTRY NO.: 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7665-99-8 (Cyclic GMP)
CHEMICAL NAME: 0 (Bacterial Proteins); EC 3.2.1.23 (beta-Galactosidase)

L98 ANSWER 14 OF 39 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2007528248 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17824927
TITLE: A cyclic-di-GMP receptor required for bacterial exopolysaccharide production.
AUTHOR: Lee Vincent T; Matewish Jody M; Kessler Jennifer L; Hyodo Mamoru; Hayakawa Yoshihiro; Lory Stephen
CORPORATE SOURCE: Department of Microbiology and Molecular Genetics, Harvard Medical School, Boston, MA 02115, USA.
CONTRACT NUMBER: R37 AI021451 (United States NIAID)
SOURCE: Molecular microbiology, (2007 Sep) Vol. 65, No. 6, pp. 1474-84.
Journal code: 8712028. ISSN: 0950-382X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200712
ENTRY DATE: Entered STN: 11 Sep 2007
Last Updated on STN: 11 Dec 2007
Entered Medline: 6 Dec 2007

ABSTRACT:
Bis-(3',5')-cyclic-dimeric-guanosine monophosphate (c-di-GMP) has been shown to be a global regulatory molecule that modulates the reciprocal responses of bacteria to activate either virulence pathways or biofilm formation. The mechanism of c-di-GMP signal transduction, including recognition of c-di-GMP and subsequent phenotypic regulation, remain largely uncharacterized. The key components of these regulatory pathways are the various adaptor proteins (c-di-GMP receptors). There is compelling evidence suggesting that, in addition to PilZ domains, there are other unidentified c-di-GMP receptors. Here we show that the PelD protein of Pseudomonas aeruginosa is a novel c-di-GMP receptor that mediates c-di-GMP regulation of PEL polysaccharide biosynthesis. Analysis of PelD orthologues identified a number of conserved residues that are required for c-di-GMP binding as well as

synthesis of the PEL polysaccharide. Secondary structure similarities of PelD to the inhibitory site of diguanylate cyclase suggest that a common fold can act as a platform to bind c-di-GMP. The combination of a c-di-GMP binding site with a variety of output signalling motifs within one protein domain provides an explanation for the specificity for different cellular responses to this regulatory dinucleotide.

CONTROLLED TERM: Amino Acid Motifs
Amino Acid Sequence
Bacterial Proteins: ME, metabolism
Biofilms
Carrier Proteins: CH, chemistry
*Carrier Proteins: ME, metabolism
Conserved Sequence
Intracellular Signaling Peptides and Proteins: CH, chemistry
*Intracellular Signaling Peptides and Proteins: ME, metabolism
Molecular Sequence Data
Mutation: GE, genetics
Operon: GE, genetics
Phenotype
Phosphorus-Oxygen Lyases: ME, metabolism
*Polysaccharides, Bacterial: BI, biosynthesis
Protein Binding
Protein Structure, Tertiary
*Pseudomonas aeruginosa: ME, metabolism
Pseudomonas aeruginosa: PH, physiology
Signal Transduction

CAS REGISTRY NO.: 128531-82-8 (exopolysaccharide, Pseudomonas)

CHEMICAL NAME: 0 (Bacterial Proteins); 0 (Carrier Proteins); 0 (Intracellular Signaling Peptides and Proteins); 0 (Polysaccharides, Bacterial); 0 (RetS protein, Pseudomonas aeruginosa); 0 (cyclic GMP-binding protein); EC 4.6.- (Phosphorus-Oxygen Lyases); EC 4.6.1.- (diguanylate cyclase)

L98 ANSWER 15 OF 39 MEDLINE on STN DUPLICATE 6

ACCESSION NUMBER: 2008051556 IN-PROCESS Full-text

DOCUMENT NUMBER: PubMed ID: 18028314

TITLE: Subcellular location characteristics of the Pseudomonas aeruginosa GGDEF protein, WspR, indicate that it produces cyclic-di-GMP in response to growth on surfaces.

AUTHOR: Guvener Zehra Tuzun; Harwood Caroline S

CORPORATE SOURCE: Department of Microbiology, University of Washington, Seattle, WA 98195, USA.

CONTRACT NUMBER: GM56665 (United States NIGMS)

SOURCE: Molecular microbiology, (2007 Dec) Vol. 66, No. 6, pp. 1459-73. Electronic Publication: 2007-11-19. Journal code: 8712028. ISSN: 0950-382X.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, N.I.H., EXTRAMURAL)

LANGUAGE: English

FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals

ENTRY DATE: Entered STN: 23 Jan 2008
Last Updated on STN: 23 Jan 2008

ABSTRACT:

The Pseudomonas aeruginosa Wsp signal transduction system produces ***cyclic*** -di-GMP (c-di-GMP), an intracellular

messenger that stimulates biofilm formation and suppresses motility. The Wsp system is homologous to chemotaxis systems and includes a membrane-bound receptor protein, WspA, and a response regulator GGDEF protein, WspR, that catalyses c-di-GMP synthesis when phosphorylated. We found that the subcellular distributions of fluorescent protein-tagged WspA and WspR differed markedly from their chemotaxis counterparts. WspA-YFP formed patches in cells whereas WspR-YFP was dispersed when unphosphorylated and formed bright cytoplasmic clusters when phosphorylated. WspR formed clusters in cells of a DeltawspF mutant, a genetic background that causes constitutive phosphorylation of WspR, but was dispersed in cells of a wspA mutant, a genetic background necessary for WspR phosphorylation. In addition, WspR mutated at Asp70, its predicted site of phosphorylation, did not form clusters. C-di-GMP synthesis was not required for cluster formation. WspR-YFP was dispersed in liquid-grown wild-type cells, but formed clusters that sometimes appeared and disappeared over the course of a few minutes in cells grown on an agar surface. Our results suggest that the compartmentalized production of c-di-GMP in response to a stimulus associated with growth on a surface is an important functional characteristic of the Wsp system.

L98 ANSWER 16 OF 39 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2007042025 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17241199
TITLE: Cyclic di-GMP signalling in the virulence and environmental adaptation of Xanthomonas campestris.
AUTHOR: Ryan Robert P; Fouhy Yvonne; Lucey Jean F; Jiang Bo-Le; He Yong-Qiang; Feng Jia-Xun; Tang Ji-Liang; Dow J Maxwell
CORPORATE SOURCE: BIOMERIT Research Centre, Department of Microbiology, BioSciences Institute, National University of Ireland, Cork, Ireland.
SOURCE: Molecular microbiology, (2007 Jan) Vol. 63, No. 2, pp. 429-42.
Journal code: 8712028. ISSN: 0950-382X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200706
ENTRY DATE: Entered STN: 24 Jan 2007
Last Updated on STN: 20 Jun 2007
Entered Medline: 19 Jun 2007

ABSTRACT:

Cyclic di-GMP is a second messenger with a role in regulation of a range of cellular functions in diverse bacteria including the virulence of pathogens. Cellular levels of cyclic ***di*** -GMP are controlled through synthesis, catalysed by the GGDEF protein domain, and degradation by EAL or HD-GYP domains. Here we report a comprehensive study of cyclic di-GMP signalling in bacterial disease in which we examine the contribution of all proteins with GGDEF, EAL or HD-GYP domains to virulence and virulence factor production in the phytopathogen Xanthomonas campestris pathovar campestris (Xcc). Genes with significant roles in virulence to plants included those encoding proteins whose probable function is in ***cyclic*** -di-GMP synthesis as well as others (including the HD-GYP domain regulator RpfG) implicated in cyclic ***di*** -GMP degradation. Furthermore, RpfG controlled expression of a subset of these genes. A partially overlapping set of elements controlled the production of virulence factors in vitro. Other GGDEF-EAL domain proteins had no effect on virulence factor synthesis but did

influence motility. These findings indicate the existence of a regulatory network that may allow Xcc to integrate information from diverse environmental inputs to modulate virulence factor synthesis as well as of ***cyclic*** di-GMP signalling systems dedicated to other specific tasks.

CONTROLLED TERM: Adaptation, Physiological
Bacterial Proteins: BI, biosynthesis
Biofilms: GD, growth & development
DNA Transposable Elements: GE, genetics
*Gene Expression Regulation, Bacterial
*Guanine Nucleotides: ME, metabolism
Movement
Mutagenesis, Insertional
RNA, Bacterial: AN, analysis
RNA, Bacterial: GE, genetics
RNA, Messenger: AN, analysis
RNA, Messenger: GE, genetics
Raphanus: MI, microbiology
Reverse Transcriptase Polymerase Chain Reaction
*Signal Transduction
Transcription, Genetic
Virulence
Virulence Factors: BI, biosynthesis
Xanthomonas campestris: GE, genetics
Xanthomonas campestris: ME, metabolism
*Xanthomonas campestris: PY, pathogenicity

CAS REGISTRY NO.: 634-02-6 (2',3'-cyclic GMP)

CHEMICAL NAME: 0 (Bacterial Proteins); 0 (DNA Transposable Elements); 0 (Guanine Nucleotides); 0 (RNA, Bacterial); 0 (RNA, Messenger); 0 (Virulence Factors)

L98 ANSWER 17 OF 39 MEDLINE on STN DUPLICATE 9

ACCESSION NUMBER: 2006608114 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 16923812

TITLE: Allosteric control of cyclic di-GMP signaling.

AUTHOR: Christen Beat; Christen Matthias; Paul Ralf; Schmid Franziska; Folcher Marc; Jenoe Paul; Meuwly Markus; Jenal Urs

CORPORATE SOURCE: Biozentrum, University of Basel, Switzerland.

SOURCE: The Journal of biological chemistry, (2006 Oct 20) Vol. 281, No. 42, pp. 32015-24. Electronic Publication: 2006-08-21.
Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200612

ENTRY DATE: Entered STN: 17 Oct 2006
Last Updated on STN: 19 Dec 2006
Entered Medline: 6 Dec 2006

ABSTRACT:

Cyclic di-guanosine monophosphate is a bacterial second messenger that has been implicated in biofilm formation, antibiotic resistance, and persistence of pathogenic bacteria in their animal host. Although the enzymes responsible for the regulation of cellular levels of c-di-GMP, diguanylate cyclases (DGC) and phosphodiesterases, have been identified recently, little information is available on the molecular

mechanisms involved in controlling the activity of these key enzymes or on the specific interactions of c-di-GMP with effector proteins. By using a combination of genetic, biochemical, and modeling techniques we demonstrate that an allosteric binding site for c-di-GMP (I-site) is responsible for non-competitive product inhibition of DGCs. The I-site was mapped in both multi- and single domain DGC proteins and is fully contained within the GGDEF domain itself. In vivo selection experiments and kinetic analysis of the evolved I-site mutants led to the definition of an RXXD motif as the core c-di-GMP binding site. Based on these results and based on the observation that the I-site is conserved in a majority of known and potential DGC proteins, we propose that product inhibition of DGCs is of fundamental importance for c-di-GMP signaling and cellular homeostasis. The definition of the I-site binding pocket provides an entry point into unraveling the molecular mechanisms of ligand-protein interactions involved in c-di-GMP signaling and makes DGCs a valuable target for drug design to develop new strategies against ***biofilm*** -related diseases.

CONTROLLED TERM: Allosteric Site
Amino Acid Motifs
Amino Acid Sequence
Binding Sites
Cellulose: CH, chemistry
Crystallography, X-Ray
*Cyclic GMP: CH, chemistry
Escherichia coli: EN, enzymology
Feedback, Biochemical
Molecular Sequence Data
Phosphoric Diester Hydrolases: CH, chemistry
Phosphorus-Oxygen Lyases: CH, chemistry
Salmonella enterica: EN, enzymology
Signal Transduction
CAS REGISTRY NO.: 7665-99-8 (Cyclic GMP); 9004-34-6 (Cellulose)
CHEMICAL NAME: EC 3.1.4.- (Phosphoric Diester Hydrolases); EC 4.6.- (Phosphorus-Oxygen Lyases); EC 4.6.1.- (diguanylate cyclase)

L98 ANSWER 18 OF 39 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2006708493 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17028282
TITLE: Cyclic di-GMP signaling in bacteria: recent advances and new puzzles.
AUTHOR: Ryan Robert P; Fouhy Yvonne; Lucey Jean F; Dow J Maxwell
CORPORATE SOURCE: BIOMERIT Research Centre, Department of Microbiology, BioSciences Institute, National University of Ireland, Cork, Ireland.
SOURCE: Journal of bacteriology, (2006 Dec) Vol. 188, No. 24, pp. 8327-34. Electronic Publication: 2006-10-06. Ref: 65
Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200701
ENTRY DATE: Entered STN: 6 Dec 2006
Last Updated on STN: 17 Jan 2007
Entered Medline: 16 Jan 2007
CONTROLLED TERM: Animals
Bacteria: GE, genetics
Bacteria: GD, growth & development

Bacteria: ME, metabolism
Bacteria: PY, pathogenicity
Bacterial Infections: MI, microbiology
Bacterial Proteins: GE, genetics
Bacterial Proteins: ME, metabolism
*Cyclic GMP: ME, metabolism
*Gene Expression Regulation, Bacterial
Plant Diseases: MI, microbiology
*Signal Transduction
Virulence
CAS REGISTRY NO.: 7665-99-8 (Cyclic GMP)
CHEMICAL NAME: 0 (Bacterial Proteins)

L98 ANSWER 19 OF 39 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2006616909 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17050921
TITLE: BdlA, a chemotaxis regulator essential for biofilm dispersion in Pseudomonas aeruginosa.
AUTHOR: Morgan Ryan; Kohn Steven; Hwang Sung-Hei; Hassett Daniel J; Sauer Karin
CORPORATE SOURCE: Department of Biological Sciences, Binghamton University, SUNY at Binghamton, 104 Science III, NY 13902, USA.
CONTRACT NUMBER: AI-40541 (United States NIAID)
GM-69845 (United States NIGMS)
HL073835-01 (United States NHLBI)
SOURCE: Journal of bacteriology, (2006 Nov) Vol. 188, No. 21, pp. 7335-43.
Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200612
ENTRY DATE: Entered STN: 20 Oct 2006
Last Updated on STN: 19 Dec 2006
Entered Medline: 4 Dec 2006

ABSTRACT:
Multiple environmental cues have been shown to trigger biofilm detachment, the transition from surface-attached, highly organized communities known as biofilms to the motile lifestyle. The goal of this study was to identify a gene product involved in sensing environmental cues that trigger biofiim dispersion in Pseudomonas aeruginosa. To do so, we focused on novel putative chemotaxis transducer proteins that could potentially be involved in environmental sensing. We identified a locus encoding such a protein that played a role in detachment, as indicated by the observation that an isogenic mutant biofilm could not disperse in response to a variety of environmental cues. The locus was termed bdlA for biofilm dispersion locus. The BdlA protein harbors an MCP (methyl-accepting chemotaxis protein) domain and two PAS (Per-Arnt-Sint) domains that have been shown to be essential for responding to environmental signals in other proteins. The dispersion-deficient phenotype of the bdlA mutant was confirmed by treatment with the biocide H(2)O(2) and by microscopic observations. The dispersion response was independent of motility. bdlA mutant biofilms were found to have increased adherent properties and increased intracellular levels of ***cyclic*** di-GMP (c-di-GMP). Our findings suggest that BdlA may be a link between sensing environmental cues, c-di-GMP levels, and detachment. Based on our findings, a possible involvement of BdlA in a

signaling cascade resulting in biofilm dispersion is discussed.
CONTROLLED TERM: *Adaptation, Physiological
Anti-Bacterial Agents: PD, pharmacology
Bacterial Adhesion: GE, genetics
Bacterial Proteins: GE, genetics
*Bacterial Proteins: PH, physiology
*Biofilms
*Chemotaxis: GE, genetics
Cytoplasm: CH, chemistry
Gene Deletion
Guanine Nucleotides: AN, analysis
Hydrogen Peroxide: PD, pharmacology
Microscopy
Models, Biological
Movement
Mutagenesis, Insertional
Protein Structure, Tertiary
Pseudomonas aeruginosa: GE, genetics
*Pseudomonas aeruginosa: PH, physiology
*Signal Transduction
CAS REGISTRY NO.: 634-02-6 (2',3'-cyclic GMP); 7722-84-1 (Hydrogen Peroxide)
CHEMICAL NAME: 0 (Anti-Bacterial Agents); 0 (Bacterial Proteins); 0 (Guanine Nucleotides)

L98 ANSWER 20 OF 39 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 2006235070 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16611728
TITLE: Cell-cell signaling in Xanthomonas campestris involves an HD-GYP domain protein that functions in cyclic di-GMP turnover.
AUTHOR: Ryan Robert P; Fouhy Yvonne; Lucey Jean F; Crossman Lisa C; Spiro Stephen; He Ya-Wen; Zhang Lian-Hui; Heeb Stephan; Camara Miguel; Williams Paul; Dow J Maxwell
CORPORATE SOURCE: BIOMERIT Research Centre, Department of Microbiology, BioSciences Institute, National University of Ireland, Cork, Ireland.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2006 Apr 25) Vol. 103, No. 17, pp. 6712-7. Electronic Publication: 2006-04-12.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200606
ENTRY DATE: Entered STN: 28 Apr 2006
Last Updated on STN: 16 Jun 2006
Entered Medline: 15 Jun 2006
ABSTRACT:
HD-GYP is a protein domain of unknown biochemical function implicated in bacterial signaling and regulation. In the plant pathogen Xanthomonas campestris pv. campestris, the synthesis of virulence factors and dispersal of biofilms are positively controlled by a two-component signal transduction system comprising the HD-GYP domain regulatory protein RpfG and cognate sensor RpfC and by cell-cell signaling mediated by the diffusible signal molecule DSF (diffusible signal factor). The RpfG/RpfC two-component system has been implicated in DSF perception and signal transduction. Here we show that the role of RpfG is to degrade the unusual nucleotide cyclic ***di*** -GMP, an activity associated with the HD-GYP domain.

Mutation of the conserved H and D residues of the isolated HD-GYP domain resulted in loss of both the enzymatic activity against cyclic ***di*** -GMP and the regulatory activity in virulence factor synthesis. Two other protein domains, GGDEF and EAL, are already implicated in the synthesis and degradation respectively of cyclic ***di*** -GMP. As with GGDEF and EAL domains, the HD-GYP domain is widely distributed in free-living bacteria and occurs in plant and animal pathogens, as well as beneficial symbionts and organisms associated with a range of environmental niches. Identification of the role of the HD-GYP domain thus increases our understanding of a signaling network whose importance to the lifestyle of diverse bacteria is now emerging.

CONTROLLED TERM: Amino Acid Sequence
Bacterial Proteins: CH, chemistry
Bacterial Proteins: GE, genetics
*Bacterial Proteins: ME, metabolism
Base Sequence
*Cyclic GMP: AA, analogs & derivatives
Cyclic GMP: ME, metabolism
DNA, Bacterial: GE, genetics
Genes, Bacterial
Mutagenesis, Site-Directed
Mutation
Protein Structure, Tertiary
Pseudomonas aeruginosa: GE, genetics
Pseudomonas aeruginosa: ME, metabolism
Recombinant Proteins: CH, chemistry
Recombinant Proteins: GE, genetics
Recombinant Proteins: ME, metabolism
Signal Transduction
Virulence: GE, genetics
Virulence: PH, physiology
Xanthomonas campestris: GE, genetics
*Xanthomonas campestris: ME, metabolism
Xanthomonas campestris: PY, pathogenicity

CAS REGISTRY NO.: 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7665-99-8 (Cyclic GMP)

CHEMICAL NAME: 0 (Bacterial Proteins); 0 (DNA, Bacterial); 0 (Recombinant Proteins); 0 (RpfG protein, Xanthomonas campestris)

L98 ANSWER 21 OF 39 MEDLINE on STN DUPLICATE 15

ACCESSION NUMBER: 2006630000 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 17014498

TITLE: Biofilm formation and cellulose expression among diverse environmental Pseudomonas isolates.

AUTHOR: Ude Susanne; Arnold Dawn L; Moon Christina D; Timms-Wilson Tracey; Spiers Andrew J

CORPORATE SOURCE: Department of Plant Sciences, University of Oxford, South Parks Road, Oxford OX1 3RB, UK.

SOURCE: Environmental microbiology, (2006 Nov) Vol. 8, No. 11, pp. 1997-2011.
Journal code: 100883692. ISSN: 1462-2912.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200611

ENTRY DATE: Entered STN: 27 Oct 2006
Last Updated on STN: 19 Dec 2006
Entered Medline: 22 Nov 2006

ABSTRACT:

The ability to form biofilms is seen as an increasingly important ***colonization*** strategy among both pathogenic and environmental bacteria. A survey of 185 plant-associated, phytopathogenic, soil and river Pseudomonas isolates resulted in 76% producing biofilms at the air-liquid (A-L) interface after selection in static microcosms. Considerable variation in ***biofilm*** phenotype was observed, including waxy aggregations, viscous and floccular masses, and physically cohesive biofilms with continuously varying strengths over 1500-fold. Calcofluor epifluorescent microscopy identified cellulose as the matrix component in biofilms produced by Pseudomonas asplenii, Pseudomonas corrugata, Pseudomonas fluorescens, Pseudomonas marginalis, Pseudomonas putida, Pseudomonas savastanoi and Pseudomonas syringae isolates. Cellulose expression and biofilm formation could be induced by the constitutively active WspR19 mutant of the ***cyclic*** -di-GMP-associated, GGDEF domain-containing response regulator involved in the P. fluorescens SBW25 wrinkly spreader phenotype and cellular aggregation in Pseudomonas aeruginosa PA01. WspR19 could also induce P. putida KT2440, which otherwise did not produce a ***biofilm*** or express cellulose, as well as Escherichia coli K12 and Salmonella typhimurium LT2, both of which express cellulose yet lack WspR homologues. Statistical analysis of biofilm parameters suggest that ***biofilm*** development is a more complex process than that simply described by the production of attachment and matrix components and bacterial growth. This complexity was also seen in multivariate analysis as a species-ecological habitat effect, underscoring the fact that in vitro ***biofilms*** are abstractions of those surface and volume ***colonization*** processes used by bacteria in their natural environments.

CONTROLLED TERM: Bacterial Adhesion
Biofilms: CL, classification
*Biofilms: GD, growth & development
*Cellulose: BI, biosynthesis
Ecosystem
*Environmental Microbiology
Humans
Phenotype
Plants: MI, microbiology
Pseudomonas: CL, classification
*Pseudomonas: IP, isolation & purification
Pseudomonas: ME, metabolism
*Pseudomonas: PH, physiology
Soil Microbiology
Water Microbiology

CAS REGISTRY NO.: 9004-34-6 (Cellulose)

L98 ANSWER 22 OF 39 MEDLINE on STN DUPLICATE 17

ACCESSION NUMBER: 2006111619 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16497924
TITLE: Bacterial small-molecule signaling pathways.
AUTHOR: Camilli Andrew; Bassler Bonnie L
CORPORATE SOURCE: Howard Hughes Medical Institute, 136 Harrison Avenue, Boston, MA 02111-1817, USA.
SOURCE: Science (New York, N.Y.), (2006 Feb 24) Vol. 311, No. 5764, pp. 1113-6. Ref: 38
Journal code: 0404511. E-ISSN: 1095-9203.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200603
ENTRY DATE: Entered STN: 28 Feb 2006
Last Updated on STN: 17 Mar 2006
Entered Medline: 16 Mar 2006

ABSTRACT:
Bacteria use diverse small molecules for extra- and intracellular signaling. They scan small-molecule mixtures to access information about both their extracellular environment and their intracellular physiological status, and based on this information, they continuously interpret their circumstances and react rapidly to changes. Bacteria must integrate extra- and intracellular signaling information to mount appropriate responses to changes in their environment. We review recent research into two fundamental bacterial small-molecule signaling pathways: extracellular quorum-sensing signaling and intracellular cyclic dinucleotide signaling. We suggest how these two pathways may converge to control complex processes including multicellularity, biofilm formation, and virulence. We also outline new questions that have arisen from recent studies in these fields.

CONTROLLED TERM:
*4-Butyrolactone: AA, analogs & derivatives
4-Butyrolactone: ME, metabolism
*Bacterial Physiology
Bacterial Proteins: ME, metabolism
Biofilms: GD, growth & development
*Cyclic GMP: AA, analogs & derivatives
Cyclic GMP: ME, metabolism
Gene Expression Regulation, Bacterial
Genes, Bacterial
*Homoserine: AA, analogs & derivatives
Homoserine: ME, metabolism
*Lactones: ME, metabolism
Models, Biological
Oligopeptides: ME, metabolism
Phosphoric Diester Hydrolases: ME, metabolism
Phosphorus-Oxygen Lyases: ME, metabolism
Purine Nucleotides: ME, metabolism
Quinolones: ME, metabolism
Second Messenger Systems
*Signal Transduction
Virulence: GE, genetics

CAS REGISTRY NO.: 1192-20-7 (homoserine lactone); 498-19-1 (Homoserine); 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7665-99-8 (Cyclic GMP); 96-48-0 (4-Butyrolactone)

CHEMICAL NAME: 0 (2-heptyl-3-hydroxy-4-quinolone); 0 (Bacterial Proteins); 0 (Lactones); 0 (N-octanoylhomoserine lactone); 0 (Oligopeptides); 0 (Purine Nucleotides); 0 (Quinolones); EC 3.1.4.- (Phosphoric Diester Hydrolases); EC 4.6.- (Phosphorus-Oxygen Lyases); EC 4.6.1.- (diguanylate cyclase)

L98 ANSWER 23 OF 39 MEDLINE on STN DUPLICATE 23
ACCESSION NUMBER: 2005494495 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16166544
TITLE: Phenotypic convergence mediated by GGDEF-domain-containing proteins.
AUTHOR: Simm Roger; Fetherston Jacqueline D; Kader Abdul; Romling Ute; Perry Robert D
CORPORATE SOURCE: Department of Microbiology, Immunology, and Molecular Genetics, MS415 Medical Center, University of Kentucky, Lexington, KY 40536-0298, USA.
CONTRACT NUMBER: AI25098 (United States NIAID)

SOURCE: Journal of bacteriology, (2005 Oct) Vol. 187, No. 19, pp. 6816-23.
Journal code: 2985120R. ISSN: 0021-9193.
COMMENT: Erratum in: J Bacteriol. 2006 Mar;188(5):2024
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200510
ENTRY DATE: Entered STN: 17 Sep 2005
Last Updated on STN: 26 Oct 2005
Entered Medline: 25 Oct 2005

ABSTRACT:
GGDEF domain-containing proteins have been implicated in bacterial signal transduction and synthesis of the second messenger molecule cyclic-***di*** -GMP. A number of GGDEF proteins are involved in controlling the formation of extracellular matrices. AdrA (Salmonella enterica serovar Typhimurium) and HmsT (Yersinia pestis) contain GGDEF domains and are required for extracellular cellulose production and biofilm formation, respectively. Here we show that hmsT is able to restore cellulose synthesis to a Salmonella serovar Typhimurium adrA mutant and that adrA can replace hmsT in Y. pestis Hms-dependent biofilm formation. Like Y. pestis HmsT overproducers, Y. pestis cells carrying adrA under the control of an arabinose-inducible promoter produced substantial biofilms in the presence of arabinose. Finally, we demonstrate that HmsT is involved in the synthesis of cyclic di-GMP.

CONTROLLED TERM: *Bacterial Proteins: GE, genetics
Bacterial Proteins: ME, metabolism
Biofilms
Cyclic GMP: AA, analogs & derivatives
Cyclic GMP: ME, metabolism
Genetic Complementation Test
Phenotype
Plasmids
Protein Structure, Tertiary
*Salmonella typhimurium: GE, genetics
Salmonella typhimurium: ME, metabolism
*Signal Transduction: PH, physiology
*Yersinia pestis: GE, genetics
Yersinia pestis: ME, metabolism
CAS REGISTRY NO.: 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7665-99-8 (Cyclic GMP)
CHEMICAL NAME: 0 (Bacterial Proteins); 0 (HMST protein, Yersinia pestis)

L98 ANSWER 24 OF 39 MEDLINE on STN DUPLICATE 24
ACCESSION NUMBER: 2005445992 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16113306
TITLE: Cyclic diguanylate regulates Vibrio cholerae virulence gene expression.
AUTHOR: Tischler Anna D; Camilli Andrew
CORPORATE SOURCE: Department of Molecular Biology and Microbiology, Tufts University School of Medicine, 136 Harrison Avenue, Boston, Massachusetts 02111, USA.
CONTRACT NUMBER: AI45746 (United States NIAID)
P30 DK34928 (United States NIDDK)
SOURCE: Infection and immunity, (2005 Sep) Vol. 73, No. 9, pp. 5873-82.

Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200510
ENTRY DATE: Entered STN: 23 Aug 2005
Last Updated on STN: 13 Oct 2005
Entered Medline: 12 Oct 2005

ABSTRACT:
The cyclic dinucleotide second messenger cyclic diguanylate (c-diGMP) has been implicated in regulation of cell surface properties in several bacterial species, including Vibrio cholerae. Expression of genes required for V. cholerae biofilm formation is activated by an increased intracellular c-diGMP concentration. The response regulator VieA, which contains a domain responsible for degradation of c-diGMP, is required to maintain a low concentration of c-diGMP and repress biofilm formation. The VieSAB three-component signal transduction system was, however, originally identified as a regulator of ctxAB, the genes encoding cholera toxin (CT). Here we show that the c-diGMP phosphodiesterase activity of VieA is required to enhance CT production. This regulation occurred at the transcriptional level, and ectopically altering the c-diGMP concentration by expression of diguanylate cyclase or phosphodiesterase enzymes also affected ctxAB transcription. The c-diGMP phosphodiesterase activity of VieA was also required for maximal transcription toxT but did not influence the activity of ToxR or expression of TcpP. Finally, a single amino acid substitution in VieA that increases the intracellular c-diGMP concentration led to attenuation in the infant mouse model of cholera. Since virulence genes including toxT and ctxA are repressed by a high concentration of c-diGMP, while ***biofilm*** genes are activated, we suggest that c-diGMP signaling is important for the transition of V. cholerae from the environment to the host.

CONTROLLED TERM: Bacterial Proteins: GE, genetics
Bacterial Proteins: ME, metabolism
Bacterial Proteins: PH, physiology
Cholera Toxin: BI, biosynthesis
*Cyclic GMP: AA, analogs & derivatives
Cyclic GMP: CH, chemistry
Cyclic GMP: PH, physiology
*Gene Expression Regulation, Bacterial
Gene Expression Regulation, Bacterial: PH, physiology
Transcription Factors: GE, genetics
Transcription Factors: ME, metabolism
Transcription, Genetic: PH, physiology
*Vibrio cholerae: GE, genetics
Vibrio cholerae: ME, metabolism
Vibrio cholerae: PY, pathogenicity
Virulence: GE, genetics
CAS REGISTRY NO.: 147979-50-8 (tcpN protein, Vibrio cholerae); 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7665-99-8 (Cyclic GMP); 9012-63-9 (Cholera Toxin)
CHEMICAL NAME: 0 (Bacterial Proteins); 0 (Transcription Factors); 0 (VieA protein, Vibrio cholerae)

L98 ANSWER 25 OF 39 MEDLINE on STN DUPLICATE 25
ACCESSION NUMBER: 2005453894 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16121184
TITLE: Aminoglycoside antibiotics induce bacterial biofilm

formation.
AUTHOR: Hoffman Lucas R; D'Argenio David A; MacCoss Michael J; Zhang Zhaoying; Jones Roger A; Miller Samuel I
CORPORATE SOURCE: Department of Pediatrics, University of Washington, Seattle, Washington 98195, USA.
SOURCE: Nature, (2005 Aug 25) Vol. 436, No. 7054, pp. 1171-5. Journal code: 0410462. E-ISSN: 1476-4687.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, N.I.H., EXTRAMURAL) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200509
ENTRY DATE: Entered STN: 26 Aug 2005
Last Updated on STN: 9 Sep 2005
Entered Medline: 8 Sep 2005

ABSTRACT:
Biofilms are adherent aggregates of bacterial cells that form on biotic and abiotic surfaces, including human tissues. Biofilms resist antibiotic treatment and contribute to bacterial persistence in chronic infections. Hence, the elucidation of the mechanisms by which biofilms are formed may assist in the treatment of chronic infections, such as Pseudomonas aeruginosa in the airways of patients with cystic fibrosis. Here we show that subinhibitory concentrations of aminoglycoside antibiotics induce ***biofilm*** formation in P. aeruginosa and Escherichia coli. In P. aeruginosa, a gene, which we designated aminoglycoside response regulator (arr), was essential for this induction and contributed to biofilm -specific aminoglycoside resistance. The arr gene is predicted to encode an inner-membrane phosphodiesterase whose substrate is cyclic di -guanosine monophosphate (c-di-GMP)-a bacterial second messenger that regulates cell surface adhesiveness. We found that membranes from arr mutants had diminished c-di-GMP phosphodiesterase activity, and P. aeruginosa cells with a mutation changing a predicted catalytic residue of Arr were defective in their biofilm response to tobramycin. Furthermore, tobramycin-inducible biofilm formation was inhibited by exogenous GTP, which is known to inhibit c-di-GMP phosphodiesterase activity. Our results demonstrate that biofilm formation can be a specific, defensive reaction to the presence of antibiotics, and indicate that the molecular basis of this response includes alterations in the level of c-di-GMP.
CONTROLLED TERM: *Aminoglycosides: PD, pharmacology
*Anti-Bacterial Agents: PD, pharmacology
*Bacteria: DE, drug effects
Bacteria: GE, genetics
*Bacteria: GD, growth & development
Bacteria: ME, metabolism
Bacterial Proteins: GE, genetics
Bacterial Proteins: ME, metabolism
*Biofilms: DE, drug effects
*Biofilms: GD, growth & development
Cyclic GMP: AA, analogs & derivatives
Cyclic GMP: ME, metabolism
Drug Resistance, Bacterial: GE, genetics
Escherichia coli: DE, drug effects
Escherichia coli: GD, growth & development
Genes, Bacterial: GE, genetics
Genetic Complementation Test
Phenotype
Pseudomonas aeruginosa: DE, drug effects

Pseudomonas aeruginosa: GE, genetics
Pseudomonas aeruginosa: GD, growth & development
Pseudomonas aeruginosa: ME, metabolism
Tobramycin: PD, pharmacology
CAS REGISTRY NO.: 32986-56-4 (Tobramycin); 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7665-99-8 (Cyclic GMP)
CHEMICAL NAME: 0 (Aminoglycosides); 0 (Anti-Bacterial Agents); 0 (Bacterial Proteins)

L98 ANSWER 26 OF 39 MEDLINE on STN DUPLICATE 26
ACCESSION NUMBER: 2005303223 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15935569
TITLE: The phosphodiesterase activity of the HmsP EAL domain is required for negative regulation of biofilm formation in Yersinia pestis.
AUTHOR: Bobrov Alexander G; Kirillina Olga; Perry Robert D
CORPORATE SOURCE: Department of Microbiology, Immunology and Molecular Genetics, University of Kentucky, Lexington, KY 40536-0298, USA.
CONTRACT NUMBER: AI25098 (United States NIAID)
SOURCE: FEMS microbiology letters, (2005 Jun 15) Vol. 247, No. 2, pp. 123-30.
Journal code: 7705721. ISSN: 0378-1097.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200511
ENTRY DATE: Entered STN: 14 Jun 2005
Last Updated on STN: 14 Dec 2005
Entered Medline: 21 Nov 2005

ABSTRACT:
In Yersinia pestis, biofilm formation is stimulated by HmsT, a GGDEF-domain containing protein that synthesizes cyclic-di-***GMP*** (c-di-GMP), and inhibited by HmsP, an EAL-domain protein. Only the EAL-domain portion of HmsP is required to inhibit biofilm formation. The EAL domain of HmsP was purified as a 6XHis-tag fusion protein and demonstrated to have phosphodiesterase activity using bis(p-nitrophenyl) phosphate (bis-pNPP) as a substrate. This enzymatic activity was strictly manganese dependent. A critical residue (E506) of HmsP within the EAL domain, that is required for inhibition of biofilm formation, is also essential for this phosphodiesterase activity. While the proposed function of EAL-domain proteins is to linearize c-di-GMP, this is a direct demonstration of the required phosphodiesterase activity of a purified EAL-domain protein.
CONTROLLED TERM: Bacterial Proteins: CH, chemistry
Bacterial Proteins: GE, genetics
*Bacterial Proteins: PH, physiology
*Biofilms: GD, growth & development
Coenzymes: PD, pharmacology
Down-Regulation
Manganese: PD, pharmacology
Nitrophenols: ME, metabolism
Phosphoric Diester Hydrolases: CH, chemistry
Phosphoric Diester Hydrolases: GE, genetics
*Phosphoric Diester Hydrolases: PH, physiology
Protein Structure, Tertiary
*Yersinia pestis: EN, enzymology
Yersinia pestis: GE, genetics

Yersinia pestis: PH, physiology
CAS REGISTRY NO.: 645-15-8 (bis(4-nitrophenyl)phosphate); 7439-96-5 (Manganese)
CHEMICAL NAME: 0 (Bacterial Proteins); 0 (Coenzymes); 0 (Nitrophenols); EC 3.1.4.- (Phosphoric Diester Hydrolases)

L98 ANSWER 27 OF 39 MEDLINE on STN DUPLICATE 27
ACCESSION NUMBER: 2004490873 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15458421
TITLE: Role of the GGDEF protein family in Salmonella cellulose biosynthesis and biofilm formation.
AUTHOR: Garcia Begona; Latasa Cristina; Solano Cristina; Garcia-del Portillo Francisco; Gamazo Carlos; Lasa Inigo
CORPORATE SOURCE: Instituto de Agrobiotecnologia y Recursos Naturales and Departamento de Produccion Agraria, Universidad Publica de Navarra, Pamplona-31006, Navarra, Spain.
SOURCE: Molecular microbiology, (2004 Oct) Vol. 54, No. 1, pp. 264-77.
Journal code: 8712028. ISSN: 0950-382X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 2 Oct 2004
Last Updated on STN: 20 Dec 2004
Entered Medline: 10 Dec 2004

ABSTRACT:
Salmonella enterica serovar Typhimurium is capable of producing cellulose as the main exopolysaccharide compound of the biofilm matrix. It has been shown for Gluconacetobacter xylinum that cellulose biosynthesis is allosterically regulated by bis-(3',5') cyclic diguanylic acid, whose synthesis/degradation depends on diguanylate cyclase/phosphodiesterase enzymatic activities. A protein domain, named GGDEF, is present in all diguanylate cyclase/phosphodiesterase enzymes that have been studied to date. In this study, we analysed the molecular mechanisms responsible for the failure of Salmonella typhimurium strain SL1344 to form biofilms under different environmental conditions. Using a complementation assay, we were able to identify two genes, which can restore the biofilm defect of SL1344 when expressed from the plasmid pBR328. Based on the observation that one of the genes, STM1987, contains a GGDEF domain, and the other, mlrA, indirectly controls the expression of another GGDEF protein, AdrA, we proceeded on a mutational analysis of the additional GG[DE]EF motif containing proteins of S. typhimurium. Our results demonstrated that MlrA, and thus AdrA, is required for cellulose production and biofilm formation in LB complex medium whereas STM1987 (GGDEF domain containing protein A, gcpA) is critical for biofilm formation in the nutrient-deficient medium, ATM. Insertional inactivation of the other six members of the GGDEF family (gcpB-G) showed that only deletion of yciR (gcpE) affected cellulose production and ***biofilm*** formation. However, when provided on plasmid pBR328, most of the members of the GGDEF family showed a strong dominant phenotype able to bypass the need for AdrA and GcpA respectively. Altogether, these results indicate that most GGDEF proteins of S. typhimurium are functionally related, probably by controlling the levels of the same final product (cyclic ***di*** -GMP), which include among its regulatory targets the cellulose production and biofilm formation of S. typhimurium.
CONTROLLED TERM: Amino Acid Motifs
*Bacterial Proteins: CH, chemistry
Bacterial Proteins: GE, genetics

*Bacterial Proteins: ME, metabolism
*Biofilms: GD, growth & development
*Cellulose: ME, metabolism
Culture Media
*Gene Expression Regulation, Bacterial
Multigene Family
Mutation
Salmonella typhimurium: CL, classification
Salmonella typhimurium: GE, genetics
Salmonella typhimurium: GD, growth & development
*Salmonella typhimurium: ME, metabolism
CAS REGISTRY NO.: 9004-34-6 (Cellulose)
CHEMICAL NAME: 0 (Bacterial Proteins); 0 (Culture Media)

L98 ANSWER 28 OF 39 MEDLINE on STN
ACCESSION NUMBER: 2006248631 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16672614
TITLE: Transcriptome and phenotypic responses of Vibrio cholerae to increased cyclic di-GMP level.
AUTHOR: Beyhan Sinem; Tischler Anna D; Camilli Andrew; Yildiz Fitnat H
CORPORATE SOURCE: Department of Environmental Toxicology, University of California, Santa Cruz, 95064, USA.
CONTRACT NUMBER: AI055987 (United States NIAID)
SOURCE: Journal of bacteriology, (2006 May) Vol. 188, No. 10, pp. 3600-13.
Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200606
ENTRY DATE: Entered STN: 5 May 2006
Last Updated on STN: 21 Jun 2006
Entered Medline: 20 Jun 2006

ABSTRACT:
Vibrio cholerae, the causative agent of cholera, is a facultative human pathogen with intestinal and aquatic life cycles. The capacity of V. cholerae to recognize and respond to fluctuating parameters in its environment is critical to its survival. In many microorganisms, the second messenger, 3',5'-cyclic diguanylic acid (c-di-GMP), is believed to be important for integrating environmental stimuli that affect cell physiology. Sequence analysis of the V. cholerae genome has revealed an abundance of genes encoding proteins with either GGDEF domains, EAL domains, or both, which are predicted to modulate cellular c-di-GMP concentrations. To elucidate the cellular processes controlled by c-di-GMP, whole-genome transcriptome responses of the El Tor and classical V. cholerae biotypes to increased c-di-GMP concentrations were determined. The results suggest that V. cholerae responds to an elevated level of c-di-GMP by increasing the transcription of the vps, eps, and msh genes and decreasing that of flagellar genes. The functions of other c-di-GMP-regulated genes in V. cholerae are yet to be identified.
CONTROLLED TERM: Biofilms
*Cyclic GMP: AA, analogs & derivatives
Cyclic GMP: GE, genetics
Cyclic GMP: ME, metabolism
Genotype
Kinetics

Phenotype
*Transcription, Genetic
*Vibrio cholerae: GE, genetics
Vibrio cholerae: GD, growth & development
CAS REGISTRY NO.: 61093-23-0 (bis(3',5')-cyclic diguanylic acid); 7665-99-8 (Cyclic GMP)

L98 ANSWER 29 OF 39 PASCAL COPYRIGHT 2008 INIST-CNRS. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2008-0015949 PASCAL Full-text
COPYRIGHT NOTICE: Copyright .COPYRGT. 2008 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): BifA, a cyclic-di-GMP phosphodiesterase, inversely regulates biofilm formation and swarming motility by Pseudomonas aeruginosa PA14 : Biofilms 2007: broadened horizon and new emphases
AUTHOR: KUCHMA Sherry L.; BROTHERS Kimberly M.; MERRITT Judith H.; LIBERATI Nicole T.; AUSUBEL Frederick M.; O'TOOLE George A.
CORPORATE SOURCE: Department of Microbiology and Immunology, Dartmouth Medical School, Room 505, Vail Building, North College Street, Hanover, New Hampshire 03755, United States; Department of Genetics, Harvard Medical School, Boston, Massachusetts 02114, United States; Department of Molecular Biology, Massachusetts General Hospital, Boston, Massachusetts 02114, United States
SOURCE: Journal of bacteriology, (2007), 189(22), 8165-8178, 56 refs.
Conference: 4 AMS (American Society for Microbiology) Conference on Biofilms, Quebec City, Quebec (Canada), 25 Mar 2007
ISSN: 0021-9193 CODEN: JOBAAY
DOCUMENT TYPE: Journal; Conference
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-2041, 354000174213230250
ABSTRACT: The intracellular signaling molecule, cyclic -di-GMP (c-di-GMP), has been shown to influence bacterial behaviors, including motility and biofilm formation. We report the identification and characterization of PA4367, a gene involved in regulating surface-associated behaviors in Pseudomonas aeruginosa. The PA4367 gene encodes a protein with an EAL domain, associated with c-di-GMP phosphodiesterase activity, as well as a GGDEF domain, which is associated with a c-di-GMP-synthesizing diguanylate cyclase activity. Deletion of the PA4367 gene results in a severe defect in swarming motility and a hyperbiofilm phenotype; thus, we designate this gene bifA, for biofilm formation. We show that BifA localizes to the inner membrane and, in biochemical studies, that purified BifA protein exhibits phosphodiesterase activity in vitro but no detectable diguanylate cyclase activity. Furthermore, mutational analyses of the conserved EAL and GGDEF residues of BifA suggest that both domains are important for the observed phosphodiesterase activity. Consistent with these data, the ΔbifA mutant exhibits increased cellular pools of c-di-GMP relative to the wild type and increased synthesis of a polysaccharide produced by the pel locus. This increased polysaccharide production is required for the enhanced biofilm formed by the ΔbifA mutant but does not contribute to the observed swarming defect. The ΔbifA mutation also results in decreased flagellar reversals. Based on epistasis studies with the previously described sadB gene, we propose that BifA functions upstream of SadB in the control of biofilm formation and swarming.

CLASSIFICATION CODE: 002A05B15; Life sciences; Biological sciences; Microbiology; Bacteriology
CONTROLLED TERM: Pseudomonas aeruginosa; Regulation(control); Biofilm; Motility
BROADER TERM: Pseudomonadaceae; Pseudomonadales; Bacteria

L98 ANSWER 30 OF 39 PASCAL COPYRIGHT 2008 INIST-CNRS. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2006-0038997 PASCAL Full-text

TITLE (IN ENGLISH): Aminoglycoside antibiotics induce bacterial biofilm formation
AUTHOR: HOFFMAN Lucas R.; D'ARGENIO David A.; MACCOSS Michael J.; ZHAOYING ZHANG; JONES Roger A.; MILLER Samuel I.
CORPORATE SOURCE: Department of Pediatrics, University of Washington, Seattle, Washington 98195, United States; Department of Microbiology, University of Washington, Seattle, Washington 98195, United States; Department of Genome Sciences, University of Washington, Seattle, Washington 98195, United States; Department of Chemistry and Department of Chemical Biology, Rutgers University, Piscattaway, New Jersey 08854, United States; Department of Medicine, University of Washington, Seattle, Washington 98195, United States
SOURCE: Nature : (London), (2005), 436(7054), 1171-1175, 28 refs.
ISSN: 0028-0836 CODEN: NATUAS
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United Kingdom
LANGUAGE: English
AVAILABILITY: INIST-142, 354000132349690270
ABSTRACT: Biofilms are adherent aggregates of bacterial cells that form on biotic and abiotic surfaces, including human tissues. Biofilms resist antibiotic treatment and contribute to bacterial persistence in chronic infections.sup.1.sup.,.sup.2. Hence, the elucidation of the mechanisms by which biofilms are formed may assist in the treatment of chronic infections, such as Pseudomonas aeruginosa in the airways of patients with cystic fibrosis.sup.2. Here we show that subinhibitory concentrations of aminoglycoside antibiotics induce biofilm formation in P. aeruginosa and Escherichia coli. In P. aeruginosa, a gene, which we designated aminoglycoside response regulator (arr), was essential for this induction and contributed to biofilm -specific aminoglycoside resistance. The arr gene is predicted to encode an inner-membrane phosphodiesterase whose substrate is cyclic di-guanosine monophosphate (c-di-GMP)-a bacterial second messenger that regulates cell surface adhesiveness.sup.3. We found that membranes from arr mutants had diminished c-di-GMP phosphodiesterase activity, and P. aeruginosa cells with a mutation changing a predicted catalytic residue of Arr were defective in their biofilm response to tobramycin. Furthermore, tobramycin-inducible biofilm formation was inhibited by exogenous GTP, which is known to inhibit c-di-GMP phosphodiesterase activity.sup.4. Our results demonstrate that biofilm formation can be a specific, defensive reaction to the presence of antibiotics, and indicate that the molecular basis of this response includes alterations in the level of c-di-GMP.
CLASSIFICATION CODE: 002B02S02; Life sciences; Medical sciences; Pharmacology; Infectious diseases; Bacteriology
CONTROLLED TERM: Biofilm; Formation; Sensitivity resistance; Mechanism of action; Antibiotic; Aminoglycoside; Pseudomonas aeruginosa; Escherichia coli; Tobramycin; Human; In vitro; Antibacterial agent

BROADER TERM: Pseudomonadaceae; Pseudomonadales; Bacteria; Enterobacteriaceae

L98 ANSWER 31 OF 39 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2007:284372 BIOSIS Full-text
DOCUMENT NUMBER: PREV200700290132
TITLE: DgrA is a member of a new family of cyclic diguanosine monophosphate receptors and controls flagellar motor function in Caulobacter crescentus.
AUTHOR(S): Christen, Matthias; Christen, Beat; Allan, Martin G.; Folcher, Marc; Jenoe, Paul; Grzesiek, Stephan; Jenal, Urs [Reprint Author]
CORPORATE SOURCE: Univ Basel, Bioctr, Div Mol Microbiol, Klingelbergstr 70, CH-4056 Basel, Switzerland
urs.jenal@unibas.ch
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (MAR 6 2007) Vol. 104, No. 10, pp. 4112-4117.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 2 May 2007
Last Updated on STN: 2 May 2007

ABSTRACT:Bacteria are able to switch between two mutually exclusive lifestyles, motile single cells and sedentary multicellular communities that ***colonize*** surfaces. These behavioral changes contribute to an increased fitness in structured environments and are controlled by the ubiquitous bacterial second messenger cyclic diguanosine monophosphate (c-di-GMP). In response to changing environments, fluctuating levels of c-di-GMP inversely regulate cell motility and cell surface adhesins. Although the synthesis and breakdown of c-di-GMP has been studied in detail, little is known about the downstream effector mechanisms. Using affinity chromatography, we have isolated several c-di-GMP-binding proteins from Caulobacter crescentus. One of these proteins, DgrA, is a PilZ homolog involved in mediating c-di-GMP-dependent control of C crescentus cell motility. Biochemical and structural analysis of DgrA and homologs from C crescentus, Salmonella typhimurium, and Pseudomonas aeruginosa demonstrated that this protein family represents a class of specific diguanylate receptors and suggested a general mechanism for c-di-GMP binding and signal transduction. Increased concentrations of c-di-GMP or DgrA blocked motility in C crescentus by interfering with motor function rather than flagellar assembly. We present preliminary evidence implicating the flagellar motor protein FliL in DgrA-dependent cell motility control.

CONCEPT CODE: Genetics - General 03502
Physiology - General 12002
Physiology and biochemistry of bacteria 31000
Genetics of bacteria and viruses 31500
INDEX TERMS: Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Movement and Support
INDEX TERMS: Parts, Structures, & Systems of Organisms
flagellum
INDEX TERMS: Chemicals & Biochemicals
DgrA; cyclic di-GMP
receptor; cyclic di-GMP:
synthesis, binding; diguanylate receptor
INDEX TERMS: Miscellaneous Descriptors
cell motility; signal transduction pathway; flagellar motor function

ORGANISM: Classifier
Enterobacteriaceae 06702
Super Taxa
Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria; Microorganisms
Organism Name
Escherichia coli (species)
Salmonella typhimurium (species)
Taxa Notes
Bacteria, Eubacteria, Microorganisms
ORGANISM: Classifier
Prosthecate Bacteria 08310
Super Taxa
Budding and Appendaged Bacteria; Eubacteria; Bacteria; Microorganisms
Organism Name
Caulobacter crescentus (species)
Taxa Notes
Bacteria, Eubacteria, Microorganisms
ORGANISM: Classifier
Pseudomonadaceae 06508
Super Taxa
Gram-Negative Aerobic Rods and Cocci; Eubacteria; Bacteria; Microorganisms
Organism Name
Pseudomonas aeruginosa (species)
Taxa Notes
Bacteria, Eubacteria, Microorganisms
GENE NAME: Caulobacter crescentus dgrA gene (Prosthecate Bacteria); Caulobacter crescentus recA gene (Prosthecate Bacteria)

L98 ANSWER 32 OF 39 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:642975 BIOSIS Full-text
DOCUMENT NUMBER: PREV200600635075
TITLE: When the party is over: A signal for dispersal of Pseudomonas aeruginosa biofilms.
AUTHOR(S): Romeo, Tony [Reprint Author]
CORPORATE SOURCE: Emory Univ, Sch Med, Dept Microbiol and Immunol, 3105 Rollins Res Ctr,1510 Clifton Rd NE, Atlanta, GA 30322 USA romeo@microbio.emory.edu
SOURCE: Journal of Bacteriology, (NOV 2006) Vol. 188, No. 21, pp. 7325-7327.
CODEN: JOBAAY. ISSN: 0021-9193.
DOCUMENT TYPE: Article
Editorial
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Nov 2006
Last Updated on STN: 22 Nov 2006
CONCEPT CODE: Genetics - General 03502
Genetics - Human 03508
Biochemistry studies - General 10060
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Carbohydrates 10068
Metabolism - Metabolic disorders 13020
Digestive system - Pathology 14006
Respiratory system - Physiology and biochemistry 16004
Respiratory system - Pathology 16006
Physiology and biochemistry of bacteria 31000

Genetics of bacteria and viruses 31500
Immunology - General and methods 34502
Medical and clinical microbiology - General and methods 36001
Medical and clinical microbiology - Bacteriology 36002

INDEX TERMS: Major Concepts
Infection; Gastroenterology (Human Medicine, Medical Sciences); Molecular Genetics (Biochemistry and Molecular Biophysics); Biochemistry and Molecular Biophysics

INDEX TERMS: Parts, Structures, & Systems of Organisms
immune system: immune system; lung: respiratory system

INDEX TERMS: Diseases
cystic fibrosis: respiratory system disease, genetic disease, metabolic disease, digestive system disease
Cystic Fibrosis (MeSH)

INDEX TERMS: Diseases
Pseudomonas aeruginosa infection: bacterial disease, infectious disease

INDEX TERMS: Chemicals & Biochemicals
gene: expression; mRNA [messenger RNA]; nitric oxide; polysaccharide; cellulose; cyclic di
-GMP; BdlA

INDEX TERMS: Miscellaneous Descriptors
stress response; biofilm; biofilm
matrix

ORGANISM: Classifier
Enterobacteriaceae 06702
Super Taxa
Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria; Microorganisms
Organism Name
Escherichia coli (species)
Taxa Notes
Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common): host
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGANISM: Classifier
Pseudomonadaceae 06508
Super Taxa
Gram-Negative Aerobic Rods and Cocci; Eubacteria; Bacteria; Microorganisms
Organism Name
Pseudomonas aeruginosa (species)
Taxa Notes
Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier
Vibrionaceae 06704
Super Taxa
Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria; Microorganisms
Organism Name
Shewanella oneidensis (species)

Taxa Notes
Bacteria, Eubacteria, Microorganisms
REGISTRY NUMBER: 10102-43-9 (nitric oxide)
9004-34-6 (cellulose)
GENE NAME: Escherichia coli pgaABCD gene (Enterobacteriaceae);
Escherichia coli flhDC gene (Enterobacteriaceae)

L98 ANSWER 33 OF 39 Elsevier BIOBASE COPYRIGHT 2008 Elsevier Science B.V.
on STN
ACCESSION NUMBER: 2006267217 ESBIOBASE Full-text
TITLE: Identification of a novel regulatory protein (CsrD) that targets the global regulatory RNAs CsrB and CsrC for degradation by RNase E
AUTHOR: Suzuki K.; Babitzke P.; Kushner S.R.; Romeo T.
CORPORATE SOURCE: T. Romeo, Department of Microbiology and Immunology, Emory University, School of Medicine, Atlanta, GA 30322, United States.
E-mail: romeo@microbio.emory.edu
SOURCE: Genes and Development, (15 SEP 2006), 20/18 (2605-2617), 79 reference(s)
CODEN: GEDEEP ISSN: 0890-9369 E-ISSN: 1549-5477
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT: In Escherichia coli, the global regulatory protein CsrA (carbon store regulator A) binds to leader segments of target mRNAs, affecting their translation and stability. CsrA activity is regulated by two noncoding RNAs, CsrB and CsrC, which act by sequestering multiple CsrA dimers. Here, we describe a protein (CsrD) that controls the degradation of CsrB/C RNAs. The dramatic stabilization of CsrB/C RNAs in a csrD mutant altered the expression of CsrA-controlled genes in a manner predicted from the previously described Csr regulatory circuitry. A deficiency in RNase E, the primary endonuclease involved in mRNA decay, also stabilized CsrB/C, although the half-lives of other RNAs that are substrates for RNase E (rpsO, rpsT, and RyhB) were unaffected by csrD. Analysis of the decay of CsrB RNA, both in vitro and in vivo, suggested that CsrD is not a ribonuclease. Interestingly, the CsrD protein contains GGDEF and EAL domains, yet unlike typical proteins in this large superfamily, its activity in the regulation of CsrB/C decay does not involve cyclic di- GMP metabolism. The two predicted membrane-spanning regions are dispensable for CsrD activity, while HAMP-like, GGDEF, and EAL domains are required. Thus, these studies demonstrate a novel process for the selective targeting of RNA molecules for degradation by RNase E and a novel function for a GGDEF-EAL protein. .COPYRGT. 2006 by Cold Spring Harbor Laboratory Press. CLASSIFICATION CODE: 82.2 PROTEIN BIOCHEMISTRY: STRUCTURAL STUDIES
82.8.4 PROTEIN BIOCHEMISTRY: HYDROLYTIC ENZYMES (EC 3.): Ribonucleases
SUPPLEMENTARY TERM: RNA decay; Biofilm formation; Hfq; Polynucleotide phosphorylase; Degradosome; GGDEF-EAL domain proteins
ORGANISM NAME: Escherichia coli

L98 ANSWER 34 OF 39 Elsevier BIOBASE COPYRIGHT 2008 Elsevier Science B.V.
on STN
ACCESSION NUMBER: 2005167653 ESBIOBASE Full-text
TITLE: Characterization of the rdar morphotype, a multicellular behaviour in Enterobacteriaceae
AUTHOR: Romling U.
CORPORATE SOURCE: U. Romling, Karolinska Institutet, Microbiology and Tumor Biology Center (MTC), Box 280, 171 77 Stockholm, Sweden.

E-mail: ute.romling@mtc.ki.se
SOURCE: Cellular and Molecular Life Sciences, (2005), 62/11 (1234-1246), 67 reference(s)
CODEN: CMLSFI ISSN: 1420-682X
DOCUMENT TYPE: Journal; General Review
COUNTRY: Switzerland
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT: The rdar morphotype, a multicellular behaviour of Salmonella enterica and Escherichia coli is characterized by the expression of the adhesive extracellular matrix components cellulose and curli fimbriae. The response regulator CsgD, which transcriptionally activates the biosynthesis of the exopolysaccharide cellulose and curli, also transforms cell physiology to the multicellular state. However, the only role of CsgD in cellulose biosynthesis is the activation of AdrA, a GGDEF domain protein that mediates production of the allosteric activator cyclic-di-(3'-5')guanylic acid (c-di-GMP). In S. enterica serovar Typhimurium a regulatory network consisting of 19 GGDEF/EAL domain-containing proteins tightly controls the concentration of c-di-GMP. c-di-GMP not only regulates the expression of cellulose, but also stimulates expression of adhesive curli and represses various modes of motility. Functions of characterized GGDEF and EAL domain proteins, as well as database searches, point to a global role for c-di-GMP as a novel secondary messenger that regulates a variety of cellular functions in response to diverse environmental stimuli already in the deepest roots of the prokaryotes. .COPYRGT. Birkhauser Verlag, 2005. CLASSIFICATION CODE: 84.1.8.3 GENETICS AND MOLECULAR BIOLOGY: MOLECULAR GENETICS: Gene Expression in Prokaryotes: Transcriptional regulation
85.7.7 APPLIED MICROBIOLOGY AND BIOTECHNOLOGY: MICROBIAL METABOLISM AND PHYSIOLOGY: Carbon Transport and Metabolism
SUPPLEMENTARY TERM: Biofilm; Cellulose; Curli fimbriae; Cyclic di-GMP; EAL domain; Escherichia coli; GGDEF domain; Salmonella enterica
ORGANISM NAME: Salmonella enterica; Escherichia coli; Enterobacteriaceae; Typhimurium; cellular organisms; Prokaryota

L98 ANSWER 35 OF 39 LIFESCI COPYRIGHT 2008 CSA on STN DUPLICATE 22
ACCESSION NUMBER: 2007:17256 LIFESCI Full-text
TITLE: Cyclic di-GMP signalling in the virulence and environmental adaptation of Xanthomonas campestris
AUTHOR: Dow, J.M.; Ryan, R.; Fouhy, Y.; Lucey, J.; He, Y.-Q.; Feng, J.-X.; Tang, J.-L.
CORPORATE SOURCE: University College Cork, Ireland
SOURCE: Phytopathology, (20060600) vol. 96, no. 6, p. S136. Meeting Info.: American Phytopathological Society 2006 Annual Meeting. Quebec, Quebec (Canada). 29 Jul-2 Aug 2006. ISSN: 0031-949X.
DOCUMENT TYPE: Journal
TREATMENT CODE: Conference
FILE SEGMENT: J
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT: Cyclic di-GMP is secondary messenger with a role in regulation of a range of cellular functions in diverse bacteria. Cellular levels of cyclic di-GMP are controlled through synthesis, catalysed by the GGDEF protein domain, and degradation by EAL and HD-GYP domains. We have examined the role of cyclic di-GMP signalling in disease caused by

Xanthomonas campestris pathovar campestris by examination of the contribution of all proteins with GGDEF, EAL or HD-GYP domains to virulence and virulence factor production. The sub-set of proteins with significant roles in virulence included the HD-GYP domain regulator RpfG, which is involved in signal transduction following perception of the cell-cell signal DSF. A partially overlapping set of elements controlled the production of virulence factors in vitro. Other GGDEF/EAL domain proteins had no effect on virulence factor synthesis but did influence motility. The findings indicate the existence of a regulatory network that may allow Xcc to integrate information from cell-cell signalling with other environmental inputs to modulate virulence factor synthesis as well as of cyclic di- GMP signalling systems dedicated to specific other tasks.

CLASSIFICATION: 02721 Cell cycle, morphology and motility
UNCONTROLLED TERM: Adaptations; Biodegradation; Conferences; Information processing; Motility; Perception; Signal transduction; virulence factors; Xanthomonas campestris

L98 ANSWER 36 OF 39 CONFSCI COPYRIGHT 2008 CSA on STN
ACCESSION NUMBER: 2006:59798 CONFSCI
DOCUMENT NUMBER: 06-018367
TITLE: Cyclic-di-GMP Signalling and Virulence in the Plant Pathogen Xanthomonas Campestris
AUTHOR: Ryan, R.
CORPORATE SOURCE: National University of Ireland, Cork
SOURCE: 000 0000: 158th Meeting of the Society for General Microbiology (0000000). University of Warwick, England (UK) . 3-6 Apr 2006. Society for General Microbiology (SGM).
DOCUMENT TYPE: Conference
FILE SEGMENT: DCCP
LANGUAGE: UNAVAILABLE
CLASSIFICATION: 2000 BIOLOGY GENERAL

L98 ANSWER 37 OF 39 CONFSCI COPYRIGHT 2008 CSA on STN
ACCESSION NUMBER: 2006:59119 CONFSCI
DOCUMENT NUMBER: 06-017688
TITLE: Cyclic di-GMP Regulation in Pseudomonas aeruginosa Biofilms
AUTHOR: Hoffman, Lucas R.
CORPORATE SOURCE: Univ. of Washington, Seattle, WA.
SOURCE: 000 0000: 106th General Meeting of the American Society for Microbiology (0000000). Orange County Convention Center, Orlando, Florida (USA). 21-25 May 2006. American Society for Microbiology.
DOCUMENT TYPE: Conference
FILE SEGMENT: DCCP
LANGUAGE: UNAVAILABLE
CLASSIFICATION: 2000 BIOLOGY GENERAL

L98 ANSWER 38 OF 39 BIOENG COPYRIGHT 2008 CSA on STN
ACCESSION NUMBER: 2006021676 BIOENG Full-text
DOCUMENT NUMBER: 6727058
TITLES: Bacterial Small-Molecule Signaling Pathways
AUTHOR: Camilli, Andrew; Bassler, Bonnie L
CORPORATE SOURCE: Howard Hughes Medical Institute, 136 Harrison Avenue, Boston, MA 02111-1817, USA, [mailto:bbassler@molbio.princeton.edu]

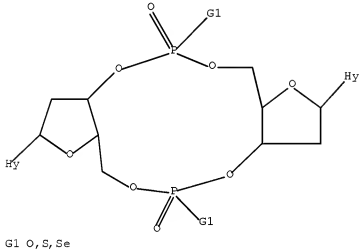
SOURCE: Science (Washington) [Science (Wash.)]. Vol. 311, no. 5764, pp. 1113-1116. 24 Feb 2006. Published by: American Association for the Advancement of Science, 1200 New York Avenue, NW Washington DC 20005 USA, [mailto:membership@aaas.org], [URL:Error! Hyperlink reference not valid. ISSN: 0036-8075
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
SUMMARY LANGUAGE: English
OTHER SOURCE: Chemoreception Abstracts
ABSTRACT: Bacteria use diverse small molecules for extra- and intracellular signaling. They scan small-molecule mixtures to access information about both their extracellular environment and their intracellular physiological status, and based on this information, they continuously interpret their circumstances and react rapidly to changes. Bacteria must integrate extra- and intracellular signaling information to mount appropriate responses to changes in their environment. We review recent research into two fundamental bacterial small-molecule signaling pathways: extracellular quorum-sensing signaling and intracellular cyclic dinucleotide signaling. We suggest how these two pathways may converge to control complex processes including multicellularity, biofilm formation, and virulence. We also outline new questions that have arisen from recent studies in these fields.
CLASSIFICATION CODE: 18008 Pheromones & other infochemicals
CONTROLLED TERMS: Intracellular signalling; Signal transduction; Virulence; Reviews; Biofilms; Bacteria

L98 ANSWER 39 OF 39 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006625193 EMBASE Full-text
TITLE: Mechanisms of cyclic-di-GMP signaling in bacteria.
AUTHOR: Jenal U.; Malone J.
CORPORATE SOURCE: U. Jenal, Biozentrum, University of Basel, CH-4056 Basel, Switzerland. urs.jenal@unibas.ch
SOURCE: Annual Review of Genetics, (2006) Vol. 40, pp. 385-407. Editor: Campell; Anderson; Jones Refs: 121 ISSN: 0066-4197 ISBN: 0824312406; 9780824312404 CODEN: ARVGB7
COUNTRY: United States
DOCUMENT TYPE: Book; Series; (Book Series); General Review; (Review)
FILE SEGMENT: 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Feb 2007 Last Updated on STN: 1 Feb 2007
ABSTRACT: Cyclic-di-GMP is a ubiquitous second messenger in bacteria. The recent discovery that c-di-GMP antagonistically controls motility and virulence of single, planktonic cells on one hand and cell adhesion and persistence of multicellular communities on the other has spurred interest in this regulatory compound. Cellular levels of c-di-GMP are controlled through the opposing activities of diguanylate cyclases and phosphodiesterases, which represent two large families of output domains found in bacterial one- and two-component systems. This review concentrates on structural and functional aspects of diguanylate cyclases and phosphodiesterases, and on their role in transmitting environmental stimuli into a range of different cellular functions. In addition, we examine several well-established model systems for c-di-GMP signaling, including Pseudomonas, Vibrio, Caulobacter, and Salmonella. Copyright .COPYRGT. 2006 by Annual

CONTROLLED TERM: Medical Descriptors:
*bacterial virulence
bacterioplankton
Caulobacter
cell adhesion
cell function
cell motility
enzyme analysis
enzyme structure
*microbial activity
nonhuman
priority journal
protein domain
protein family
Pseudomonas
review
Salmonella
second messenger
signal transduction
CONTROLLED TERM: Drug Descriptors:
*cyclic diguanosine phosphate
*cyclic GMP
diguanylate cyclase
guanylate cyclase
phosphodiesterase
CAS REGISTRY NO.: (cyclic GMP) 7665-99-8; (guanylate cyclase) 9054-75-5

SEARCH OF SPECIFIC COMPOUNDS ON pp.19-21

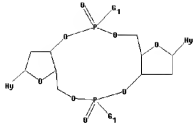
```
=> fil reg; d stat que 186
FILE 'REGISTRY' ENTERED AT 15:42:29 ON 19 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   18 MAR 2008  HIGHEST RN 1008796-87-9
DICTIONARY FILE UPDATES:  18 MAR 2008  HIGHEST RN 1008796-87-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

L8                STR
```

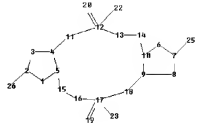


G1 O,S,Se

Structure attributes must be viewed using STN Express query preparation.

Uploading L8.str





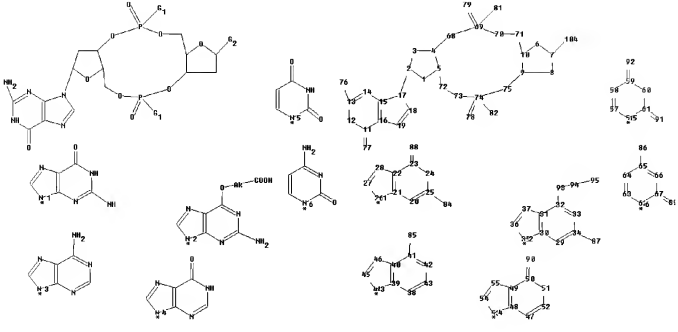
```
chain nodes :
19  20  22  23  25  26
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  17  18
chain bonds :
2-26  7-25  12-20  12-22  17-19  17-23
ring bonds :
1-2  1-5  2-3  3-4  4-5  4-11  5-15  6-7  6-10  7-8  8-9  9-10  9-18  10-14  11-12
12-13  13-14  15-16  16-17  17-18
exact/norm bonds :
1-2  1-5  2-3  2-26  3-4  4-5  4-11  5-15  6-7  6-10  7-8  7-25  8-9  9-10  9-18
10-14  11-12  12-13  12-20  12-22  13-14  15-16  16-17  17-18  17-19  17-23


G1:O,S,Se

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:CLASS
20:CLASS  22:CLASS  23:CLASS  25:CLASS  26:Atom
Generic attributes :
25:
Saturation              : Unsaturated
26:
Saturation              : Unsaturated

Element Count :
Node 25: Limited
    N,N2

Node 26: Limited
    N,N2
```

L13 136 SEA FILE=REGISTRY SSS FUL L8
L83 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

Uploading L83.str

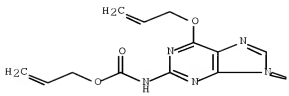


chain nodes :
76 77 78 79 81 82 84 85 86 87 88 89 90 91 92 93 94 95 104
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44
45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65
66 67 68 69 70 71 72 73 74 75
chain bonds :
2-17 7-104 11-77 13-76 23-88 25-84 32-93 34-87 41-85 50-90 59-92 61-91
65-86 67-89 69-79 69-81 74-78 74-82 93-94 94-95
ring bonds :
1-2 1-5 2-3 3-4 4-5 4-68 5-72 6-7 6-10 7-8 8-9 9-10 9-75 10-71 11-12
11-16 12-13 13-14 14-15 15-16 15-17 16-19 17-18 18-19 20-21 20-25 21-22
21-26 22-23 22-28 23-24 24-25 26-27 27-28 29-30 29-34 30-31 30-35 31-32
31-37 32-33 33-34 35-36 36-37 38-39 38-43 39-40 39-44 40-41 40-46 41-42
42-43 44-45 45-46 47-48 47-52 48-49 48-53 49-50 49-55 50-51 51-52 53-54
54-55 56-57 56-61 57-58 58-59 59-60 60-61 62-63 62-67 63-64 64-65 65-66
66-67 68-69 69-70 70-71 72-73 73-74 74-75
exact/norm bonds :
1-2 1-5 2-3 2-17 3-4 4-5 4-68 5-72 6-7 6-10 7-8 7-104 8-9 9-10 9-75
10-71 11-12 11-16 11-77 12-13 13-14 13-76 14-15 15-16 15-17 16-19 17-18
18-19 20-21 20-25 21-22 21-26 22-23 22-28 23-24 23-88 24-25 25-84 26-27
27-28 30-35 31-37 32-93 34-87 35-36 36-37 39-44 40-46 41-85 44-45 45-46
47-48 47-52 48-49 48-53 49-50 49-55 50-51 50-90 51-52 53-54 54-55 56-57
56-61 57-58 58-59 59-60 59-92 60-61 61-91 62-63 62-67 63-64 64-65 65-66
65-86 66-67 67-89 68-69 69-70 69-79 69-81 70-71 72-73 73-74 74-75 74-78
74-82 93-94 94-95
normalized bonds :

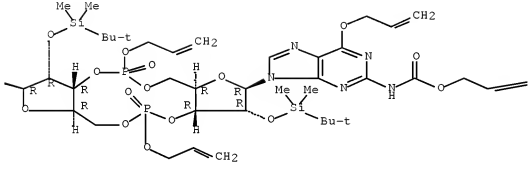
```
29-30  29-34  30-31  31-32  32-33  33-34  38-39  38-43  39-40  40-41  41-42  42-43

G1:O,S,Se

G2:[*1],[*2],[*3],[*4],[*5],[*6]

Connectivity :
94:2 E exact RC ring/chain
Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:Atom
20:Atom  21:Atom  22:Atom  23:Atom  24:Atom  25:Atom  26:Atom  27:Atom  28:Atom
29:Atom  30:Atom  31:Atom  32:Atom  33:Atom  34:Atom  35:Atom  36:Atom  37:Atom
38:Atom  39:Atom  40:Atom  41:Atom  42:Atom  43:Atom  44:Atom  45:Atom  46:Atom
47:Atom  48:Atom  49:Atom  50:Atom  51:Atom  52:Atom  53:Atom  54:Atom  55:Atom
56:Atom  57:Atom  58:Atom  59:Atom  60:Atom  61:Atom  62:Atom  63:Atom  64:Atom
65:Atom  66:Atom  67:Atom  68:Atom  69:Atom  70:Atom  71:Atom  72:Atom  73:Atom
74:Atom  75:Atom  76:CLASS  77:CLASS  78:CLASS  79:CLASS  81:CLASS  82:CLASS
84:CLASS  85:CLASS  86:CLASS  87:CLASS  88:CLASS  89:CLASS  90:CLASS  91:CLASS
92:CLASS  93:CLASS  94:CLASS  95:CLASS  104:CLASS



L86          40 SEA FILE=REGISTRY SUB=L13 SSS FUL L83

100.0% PROCESSED      58 ITERATIONS                          40 ANSWERS
SEARCH TIME: 00.00.01



=> fil capl; d que nos l88
FILE 'CAPLUS' ENTERED AT 15:42:36 ON 19 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 19 Mar 2008  VOL 148 ISS 12
FILE LAST UPDATED: 18 Mar 2008  (20080318/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE


L8              STR
```

```
L13         136 SEA FILE=REGISTRY SSS FUL L8
L14         149 SEA FILE=CAPLUS ABB=ON  L13
L30          70 SEA FILE=CAPLUS ABB=ON  L14 AND (PY<2004 OR AY<2004 OR
                PRY<2004)
L83             STR
L86          40 SEA FILE=REGISTRY SUB=L13 SSS FUL L83
L87         108 SEA FILE=CAPLUS ABB=ON  L86
L88          32 SEA FILE=CAPLUS ABB=ON  L30 AND L87


=> s l88 not l16,l92,l82,l81
L99          25 L88 NOT (L16 OR L92 OR L82 OR L81)

=> d ibib abs hitstr l99 1-25; fil hom

L99  ANSWER 1 OF 25  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2003:677651  CAPLUS  Full-text
DOCUMENT NUMBER:          140:199576
TITLE:                    A new synthetic approach to cyclic
                          bis(3'→5')diguanylic acid
AUTHOR(S):                Kawai, Rie; Nagata, Reiko; Hirata, Akiyoshi; Hayakawa,
                          Yoshihiro
CORPORATE SOURCE:         Graduate School of Human Informatics, Nagoya
                          University, Nagoya, 464-8601, Japan
SOURCE:                   Nucleic Acids Research Supplement (2003),
                          3(3rd International Symposium on Nucleic Acids
                          Chemistry [and] 30th Symposium on Nucleic Acids
                          Chemistry in Japan, 2003), 103-104
                          CODEN: NARSCE
PUBLISHER:                Oxford University Press
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   A symposium.  We developed a novel synthesis of biol. important cyclic
     bis(3'→5')diguanylic acid (cGpGp).  The present synthesis includes two
     strategies different from those employed in an existing synthesis. They are
     the phosphoramidite method for the preparation of a guanylyl(3'→5')guanylic
     acid intermediate and allyl protection for guanine bases and internucleotide
     linkages.  These distinctive strategies have allowed the new synthesis to
     provide the target compound in a higher yield than that of the existing
     synthesis.
IT   609343-81-9P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (synthesis of cyclic bis(3'→5')diguanylic acid via
        phosphoramidite method and allyl protection for guanine bases and
        internucleotide linkages)
RN   609343-81-9  CAPLUS
CN   3'-Guanylic acid, 2'-O-[(1,1-dimethylethyl)dimethylsilyl]-P-2-propenyl-6-O-
     2-propenyl-N-[(2-propenyloxy)carbonyl]guanylyl-(3'→5')-2'-O-[(1,1-
     dimethylethyl)dimethylsilyl]-6-O-2-propenyl-N-[(2-propenyloxy)carbonyl]-,
     mono-2-propenyl ester, cyclic nucleotide (9CI)  (CA INDEX NAME)

Absolute stereochemistry.
```

PAGE 1-A



PAGE 1-B

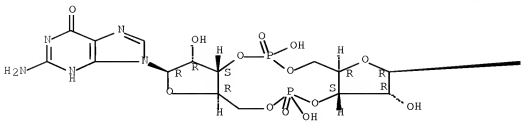


PAGE 1-C

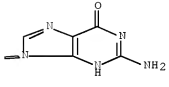
IT 61093-23-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of cyclic bis(3'→5')diguanylic acid via phosphoramidite method and allyl protection for guanine bases and internucleotide linkages)
RN 61093-23-0 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:598480 CAPLUS Full-text
DOCUMENT NUMBER: 139:292443
TITLE: A facile synthesis of cyclic bis(3'→5')diguanylic acid
AUTHOR(S): Hayakawa, Yoshihiro; Nagata, Reiko; Hirata, Akiyoshi; Hyodo, Mamoru; Kawai, Rie
CORPORATE SOURCE: Laboratory of Bioorganic Chemistry, Graduate School of Human Informatics, Nagoya University, Nagoya, 464-8601, Japan
SOURCE: Tetrahedron (2003), 59(34), 6465-6471
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:292443

AB This paper describes a new method for synthesizing biol. important cyclic bis(3'→5')diguanylic acid (cGpGp) in a higher yield than that of the existing synthetic method. In the new synthesis, the following two means, in place of those used in the existing synthesis are employed as main strategies to cause the increase in product yield. One of these distinctive strategies in the new synthesis is that the phosphoramidite method is used for the preparation of a key synthetic intermediate of a linear guanylyl(3'→5')guanylic acid derivative This method allowed higher-yield formation of the intermediate than that by the triester method used in the existing synthesis. The second distinctive strategy used in the new synthesis is that allyloxycarbonyl and allyl groups are used for the protection of two guanine bases and two internucleotide bonds, resp. These four allylic protectors can be removed all at once by the organopalladium-catalyzed reaction under neutral conditions. Thus, deprotection of the protected cGpGp precursor was achieved in the present synthesis in a shorter step and under milder conditions than the deprotection achieved in the existing synthesis, which uses diphenylacetyl and o-chlorophenyl groups as protectors for two guanine bases and two

internucleotide bonds, resp., whose full removal requires two different procedures including rather harsh basic treatment. As a result, tech. loss and decomposition of the target product in the new synthesis is remarkably reduced.

IT 609343-81-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

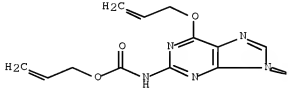
(preparation of cyclic diguanylic acid dinucleotides using allyloxycarbonyl and allyl protecting groups)

RN 609343-81-9 CAPLUS

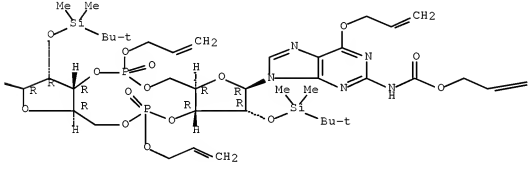
CN 3'-Guanylic acid, 2'-O-[(1,1-dimethylethyl)dimethylsilyl]-P-2-propenyl-6-O-2-propenyl-N-[(2-propenyloxy)carbonyl]guanylyl-(3'→5')-2'-O-[(1,1-dimethylethyl)dimethylsilyl]-6-O-2-propenyl-N-[(2-propenyloxy)carbonyl]-, mono-2-propenyl ester, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

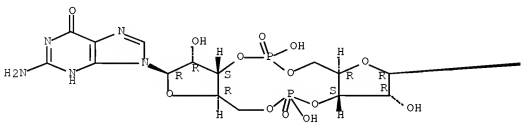


PAGE 1-C

IT 609343-62-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of cyclic diguanylic acid dinucleotides using allyloxycarbonyl and allyl protecting groups)
RN 609343-82-0 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic nucleotide, diammonium salt (9CI) (CA INDEX NAME)

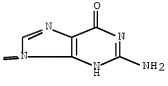
Absolute stereochemistry.

PAGE 1-A



●2 NH_3

PAGE 1-B



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:149779 CAPLUS Full-text
DOCUMENT NUMBER: 134:337461
TITLE: Phosphodiesterase A1, a Regulator of Cellulose Synthesis in Acetobacter xylinum, Is a Heme-Based Sensor
AUTHOR(S): Chang, Alan L.; Tuckerman, Jason R.; Gonzalez, Gonzalo; Mayer, Raphael; Weinhouse, Haim; Volman, Gail; Amikam, Dorit; Benziman, Moshe; Gilles-Gonzalez, Marie-Alda
CORPORATE SOURCE: Departments of Biochemistry, Plant Biology, and the Plant Biotechnology Center, The Ohio State University, Columbus, OH, 43210-1002, USA
SOURCE: Biochemistry (2001), 40(12), 3420-3426
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The phosphodiesterase A1 protein of Acetobacter xylinum, AxPDEA1, is a key regulator of bacterial cellulose synthesis. This phosphodiesterase linearizes cyclic bis(3'→5')diguanylic acid, an allosteric activator of the bacterial cellulose synthase, to the ineffectual pGpG. Here we show that AxPDEA1 contains heme and is regulated by reversible binding of O2 to the heme. Apo-AxPDEA1 has less than 2% of the phosphodiesterase activity of holo-AxPDEA1, and reconstitution with hemin restores full activity. O regulation is due to deoxyheme being a better activator than oxyheme. AxPDEA1 is homologous to the Escherichia coli direct oxygen sensor protein, EcDos, over its entire length and is homologous to the FixL histidine kinases over only a heme-binding PAS domain. The properties of the heme-binding domain of AxPDEA1 are significantly different from those of other O2-responsive heme-based sensors. The rate of AxPDEA1 autoxidn. (half-life > 12 h) is the slowest observed so far for this type of heme protein fold. The O2 affinity of AxPDEA1 (Kd .apprx. 10 μM) is comparable to that of EcDos, but the rate consts. for O2 association (kon = 6.6 μM-1 s-1) and dissociation (koff = 77 s-1) are 2000 times higher. Our results illustrate the versatility of signal transduction mechanisms for the heme-PAS class of O2 sensors and provide the first example of O2 regulation of a second messenger.

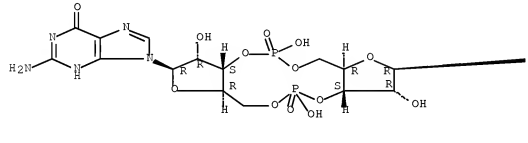
IT 61093-23-0
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Acetobacter xylinum c-di-GMP phosphodiesterase A1 activity is regulated by oxygen)

RN 61093-23-0 CAPLUS

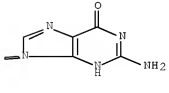
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:442449 CAPLUS Full-text
DOCUMENT NUMBER: 131:130219

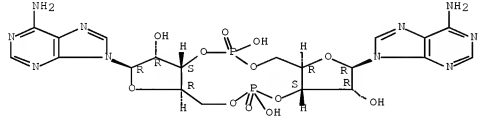
TITLE: Cyclic oligoribonucleotides (RNA) by solid-phase synthesis
AUTHOR(S): Micura, Ronald
CORPORATE SOURCE: Laboratorium fur Organische Chemie der Eidgenossischen Technischen Hochschule Universitatstrasse 16, Zurich, CH-8092, Switz.
SOURCE: Chemistry--A European Journal (1999), 5(7), 2077-2082
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel solid-phase synthesis of small- to medium-sized cyclic RNA oligonucleotides is presented. A major advantage of the approach is the lack of restrictions on the sequence variety with respect to the four standard bases adenine, cytosine, guanine, and uracil. This has been demonstrated for cycles containing 2 to 21 nucleotide units. The approach allows fully automated assembly, and is related to a procedure known for the preparation of cyclic oligonucleotides in the DNA series. It combines standard phosphoramidite chemical for chain elongation and standard phosphotriester chemical for ring closure. A key aspect of the method is use of the novel 2'-O-triisopropylsilyloxymethyl (TOM) protected RNA phosphoramidites instead of the classic tert-butyldimethylsilyl (TBDMS) protected amidites. Furthermore, the design of the final cleavage step is selective only for correctly cyclized oligoribonucleotides. This results, after deprotection, in HPLC profiles in which the crude oligonucleotide is represented by the major peak with typically more than 80% of the integrated area. The ring closure itself proceeds with an average yield of 15%.

IT 54447-84-6P 73120-97-5P 83799-66-0P
232933-52-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(cyclic oligoribonucleotides RNA by solid phase synthesis using 2'-O-triisopropylsilyloxymethyl (TOM) protecting group)

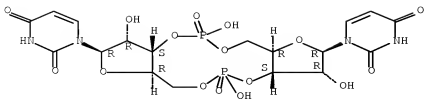
RN 54447-84-6 CAPLUS
CN 3'-Adenylic acid, adenylyl-(3'→5')-, cyclic nucleotide (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



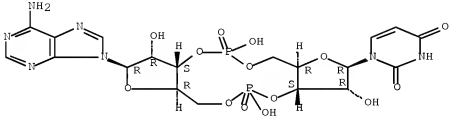
RN 73120-97-5 CAPLUS
CN 3'-Uridylic acid, uridylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



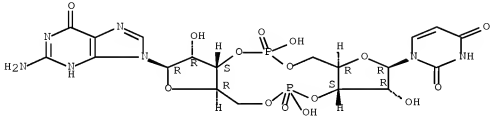
RN 83799-66-0 CAPLUS
CN 3'-Adenylic acid, uridylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 232933-52-7 CAPLUS
CN 3'-Guanylic acid, uridylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:712419 CAPLUS Full-text
DOCUMENT NUMBER: 128:11697
TITLE: c-di-GMP-binding protein, a new factor regulating cellulose synthesis in Acetobacter xylinum
AUTHOR(S): Weinhouse, Haim; Sapir, Shai; Amikam, Dorit; Shilo, Yehudit; Volman, Gail; Ohana, Patricia; Benziman, Moshe
CORPORATE SOURCE: Dep. Biol. Chemistry, Inst. Life Sciences, Hebrew Univ. Jerusalem, Jerusalem, 91904, Israel
SOURCE: FEBS Letters (1997), 416(2), 207-211

CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A protein which specifically binds cyclic diguanylic acid (c-di-GMP), the reversible allosteric activator of the membrane-bound cellulose synthase system of Acetobacter xylinum, has been identified in membrane prepns. of this organism. C-di-GMP binding is of high affinity (KD 20 nM), saturable and reversible. The equilibrium of the reaction is markedly and specifically shifted towards the binding direction by K+. The c-di-GMP binding protein, structurally associated with the cellulose synthase, appears to play a major role in modulating the intracellular concentration of free c-di-GMP and thus may constitute an essential factor in regulating cellulose synthesis in vivo.

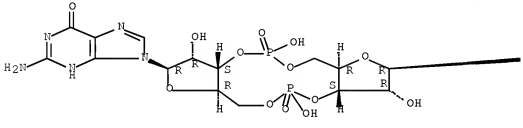
IT 61093-23-0
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cyclic diguanylate-binding protein, a new factor regulating cellulose synthesis in Acetobacter xylinum)

RN 61093-23-0 CAPLUS

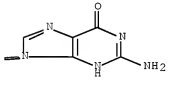
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:146808 CAPLUS Full-text
DOCUMENT NUMBER: 126:247894
TITLE: Heteronuclear scalar couplings in the bases and sugar rings of nucleic acids: their determination and application in assignment and conformational analysis
AUTHOR(S): Ippel, J. H.; Wijmenga, S. S.; de Jong, R.; Heus, H. A.; Hilbers, C. W.; de Vroom, E.; van der Marel, G. A.; van Boom, J. H.
CORPORATE SOURCE: Dep. Biophysical Chem., Univ. Nijmegen, Nijmegen, 6525

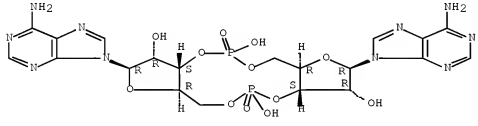
ED, Neth.
SOURCE: Magnetic Resonance in Chemistry (1996), 34(Spec. Issue), S156-S176
CODEN: MRCHEG; ISSN: 0749-1581
PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The scalar coupling consts. in uniformly isotope-enriched [13C,15N] nucleotide 5'-monophosphates (5'-NMPs) and in various non-labeled cyclic nucleotides were investigated. These model compds. yielded an almost complete set of homonuclear and heteronuclear coupling consts. in ribonucleotides, the knowledge of which is useful in designing novel heteronuclear NMR expts. and opens up new possibilities in the structure determination of larger nucleic acids. Three sets of heteronuclear coupling consts. were obtained: (1) conformation-independent 1H-13C, 1H-15N, 13C-15N, 13C-13C and 15N-15N coupling consts. in the base, knowledge of which is essential in optimizing and designing new NMR expts., which use the coherent transfer of magnetization via the J-coupling network in the nucleic acid base and sugar; (2) 1H-13C coupling consts., 3JH1'C4/2 and 3JH1'C8/6, monitoring the glycosidic torsion angle χ, give important information on the rotamer distribution around the χ angle; a new parameterization of the Karplus equations is presented; and (3) conformation-dependent one-bond and multiple bond 1H-13C coupling consts. in the ribose sugar. Conformationally rigid, cyclic, nucleotides were used to determine multiple bond 1H-13C coupling consts. in pure N-type and pure S-type sugar rings. Equations were derived for the determination of the fraction S-type sugar, pS, from the three-bond JCH couplings 3JH3'C1', 3JH2'C4', 3JH1'C3' and 3JH4'C2'. Their values for pure N- and S-type sugar conformations were used to derive Karplus equations, which describe the dependence of these coupling consts. on the phase angle, P.

IT 54447-84-6 61093-23-0 132182-16-4
RL: PRP (Properties)
(determination and application of heteronuclear scalar couplings in bases and
sugar rings of nucleic acids for assignment and conformational anal.)

RN 54447-84-6 CAPLUS
CN 3'-Adenylic acid, adenylyl-(3'→5')-, cyclic nucleotide (CA INDEX NAME)

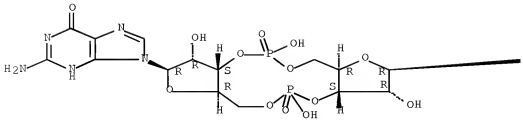
Absolute stereochemistry. Rotation (-).



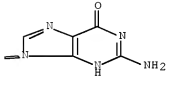
RN 61093-23-0 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



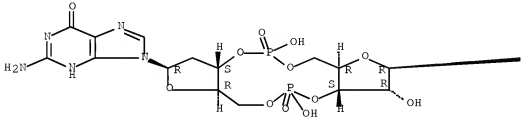
PAGE 1-B



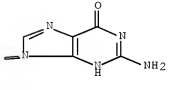
RN 132182-18-4 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L99 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:20289 CAPLUS Full-text
DOCUMENT NUMBER: 126:104351
TITLE: Synthesis of cyclic dinucleotides by an H-phosphonate method in solution
AUTHOR(S): Zeng, Fan; Jones, Roger A.
CORPORATE SOURCE: Department of Chemistry, The State University of New

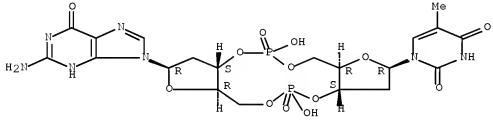
Jersey, Piscataway, NJ, 08855, USA
SOURCE: Nucleosides & Nucleotides (1996), 15(11 & 12), 1679-1686
CODEN: NUNUD5; ISSN: 0732-8311
PUBLISHER: Dekker
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We report preparation of each of the ten cyclic 2'-deoxyribodinucleotides by a solution-phase H-phosphonate method. The cyclic dimers have been characterized by 31P NMR, MS, UV, and enzymic degradation

IT 4568-15-4P 4568-39-2P 4568-41-6P
4568-42-7P 25324-45-2P 60307-63-3P
79192-34-0P 109699-00-5P 129185-16-6P
129199-02-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of cyclic dinucleotides by an H-phosphonate method in solution)

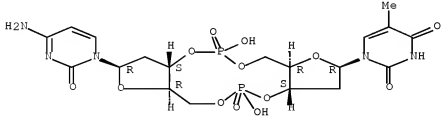
RN 4568-15-4 CAPLUS
CN 3'-Guanylic acid, thymidylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



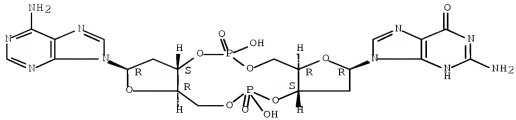
RN 4568-39-2 CAPLUS
CN 3'-Thymidylic acid, 2'-deoxycytidylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



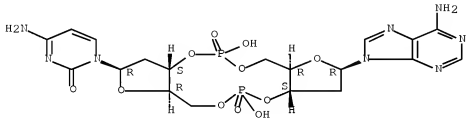
RN 4568-41-6 CAPLUS
CN 3'-Guanylic acid, 2'-deoxyadenylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



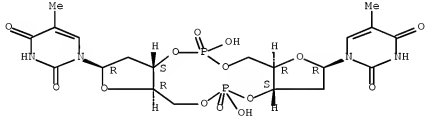
RN 4568-42-7 CAPLUS
CN 3'-Adenylic acid, 2'-deoxycytidylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 25324-45-2 CAPLUS
CN 3'-Thymidylic acid, thymidylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

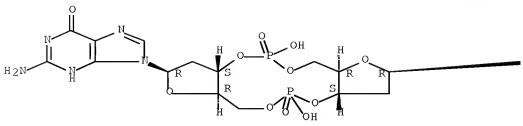
Absolute stereochemistry.



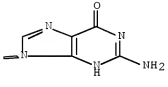
RN 60307-63-3 CAPLUS
CN 3'-Guanylic acid, 2'-deoxyguanylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



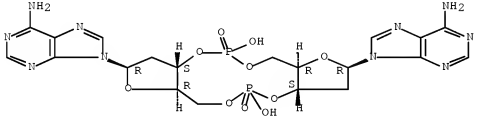
PAGE 1-B



RN 79192-34-0 CAPLUS

CN 3'-Adenylic acid, 2'-deoxyadenylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

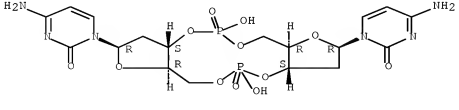
Absolute stereochemistry.



RN 109699-00-5 CAPLUS

CN 3'-Cytidylic acid, 2'-deoxycytidylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

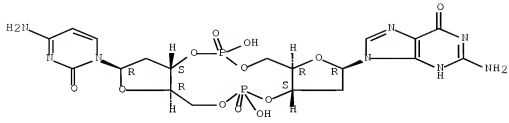


RN 129185-16-6 CAPLUS

CN 3'-Guanylic acid, 2'-deoxycytidylyl-(3'→5')-2'-deoxy-, cyclic

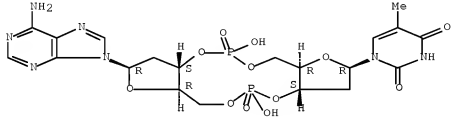
nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



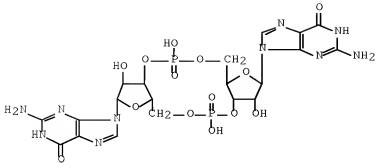
RN 129199-02-6 CAPLUS
CN 3'-Adenylic acid, thymidylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:701202 CAPLUS Full-text
DOCUMENT NUMBER: 121:301202
TITLE: Molecular structure of cyclic diguanylic acid at 1 Å resolution of two crystal forms: self-association, interactions with metal ion/planar dyes and modeling studies
AUTHOR(S): Guan, Yue; Gao, Yi Gui; Liaw, Yen Chywan; Robinson, Howard; Wang, Andrew H. J.
CORPORATE SOURCE: Div. Biophys., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Journal of Biomolecular Structure & Dynamics (1993), 11(2), 253-76
CODEN: JBSDD6; ISSN: 0739-1102
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

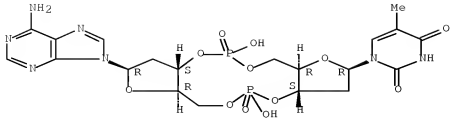
AB Cyclic ribodiguanylic acid I, is the endogenous effector regulator of cellulose synthase. Its three dimensional structure from two different crystal forms (tetragonal and trigonal) has been determined by x-ray diffraction anal. at 1 Å resolution Both structures were solved by direct methods and refined by block-matrix least squares refinement to R-factors of 0.112 (tetragonal) and 0.119 (trigonal). In both crystal forms, two independent c-(GpGp) mols. associate with each other to form a self-intercalated dimer. All four I mols. have very similar backbone conformation. The riboses are in the C3'-endo pucker with pseudorotation angles ranging from -7.2° to 16.5° and the bases have anti glycosyl χ angles (-175.5° to 179.7°). In the tetragonal form, a hydrated cobalt ion is found to coordinate to two N7 atoms of adjacent guanines, forcing these two guanines to destack with a large dihedral angle (33°). This metal coordination mechanism has been noted previously in other Pt- or Co-GMP complexes and may be relevant to the binding of the anticancer drug cisplatin to a GpG sequence in DNA. A model of the adduct between cisplatin and a d(CAATGG ATTG) duplex has been constructed in which the induced bending of the DNA helix at the Pt crosslinking site is 33°, consistent with earlier electrophoretic analyses. Moreover, I exhibits unusual spectral properties not seen in other cyclic dinucleotides. It interacts with planar organic intercalator mols. in ways similar to double helical DNA. The authors propose a cage-like model consisting of a tetrameric I aggregate in which a large cavity (host mol.) is generated to afford a binding site for certain planar intercalators (guests mols.). The aggregate likely uses a hydrogen bonding scheme the same as that found in the G-quartet mols., e.g., telomere DNA. The conformation of I also suggests that certain nearest-neighbor intercalators may be synthesized on the basis of its unique mol. framework. Modeling studies have been carried out to test this hypothesis.

IT 129199-02-6 132182-16-4 132182-20-8
132209-27-9
RL: PRP (Properties)
(absorption spectra of)

RN 129199-02-6 CAPLUS

CN 3'-Adenylic acid, thymidylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

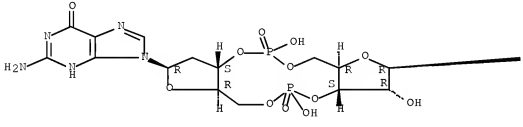


RN 132182-18-4 CAPLUS

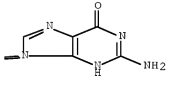
CN 3'-Guanylic acid, guanylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

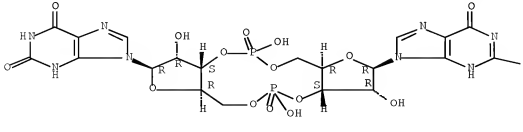


RN 132182-20-8 CAPLUS

CN 3'-Xanthylic acid, guanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



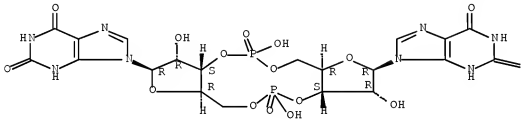
PAGE 1-B

—NH_2

RN 132209-27-9 CAPLUS
CN 3'-Xanthylic acid, xanthylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

=O

IT 158401-88-8
RL: PRP (Properties)
(crystal and mol. structure of)
RN 158401-88-8 CAPLUS
CN Cobalt(2+), hexaaqua-, (OC-6-11)-, (OC-6-22)-tetraaquabis[guanylyl-(3'→5')-3'-guanylic acid cyclic nucleotidato(2-)-κN7]cobaltate(2-) (1:1), dodecahydrate (9CI) (CA INDEX NAME)

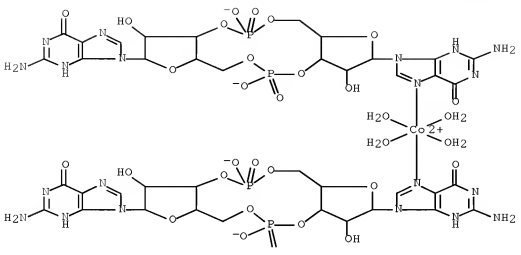
CM 1

CRN 158401-87-7
CMF C40 H52 Co N20 O32 P4 . Co H12 O6

CM 2

CRN 158401-86-6
CMF C40 H52 Co N20 O32 P4
CCI CCS

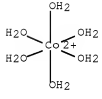
PAGE 1-A



PAGE 2-A

CM 3

CRN 15276-47-8
CMF Co H12 O6
CCI CCS



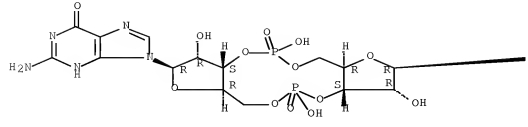
IT 153448-29-4
RL: PROC (Process)
(mol. modeling of)
RN 153448-29-4 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic nucleotide, compd. with 9-acridinamine (2:1) (9CI) (CA INDEX NAME)

CM 1

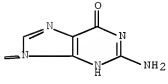
CRN 61093-23-0
CMF C20 H24 N10 O14 P2

Absolute stereochemistry.

PAGE 1-A

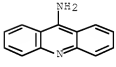


PAGE 1-B



CM 2

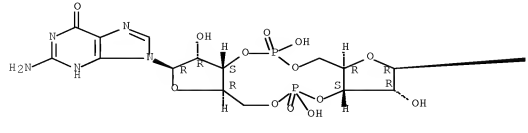
CRN 90-45-9
CMF C13 H10 N2

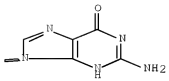


IT 61093-23-0 79192-34-0
RL: PRP (Properties)
(mol. structure of)
RN 61093-23-0 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

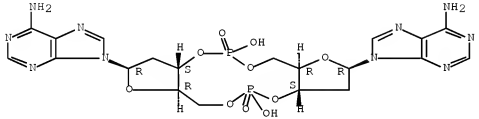
PAGE 1-A





RN 79192-34-0 CAPLUS
CN 3'-Adenylic acid, 2'-deoxyadenylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L99 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:444013 CAPLUS Full-text
DOCUMENT NUMBER: 119:44013
TITLE: β-Glucan synthesis in the cotton fiber. II. Regulation and kinetic properties of β-glucan synthases
AUTHOR(S): Li, Likun; Brown, R. Malcolm, Jr.
CORPORATE SOURCE: Dep. Bot., Univ. Texas, Austin, TX, 78713-7640, USA
SOURCE: Plant Physiology (1993), 101(4), 1143-8
CODEN: PLPHAY; ISSN: 0032-0889
DOCUMENT TYPE: Journal
LANGUAGE: English

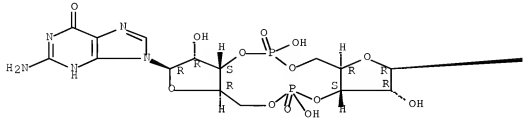
AB The regulation and kinetic properties of cellulose synthase as well as β-1,3-glucan synthase have been studied. Cellulose was detected using acetic/nitric acid insoly. as an indicator of cellulose (this product contained only β-1,4-linked glucans; K. Okuda et al., 1993). These studied reveal that (a) β-1,3-glucan synthesis is enhanced up to 31-fold by cellobiose with a Ka of 1.16 mM; (b) cellulose synthesis is increased 12-fold by a combination of cellobiose (Ka = 3.26 mM) and cyclic-3':5'-GMP (Ka = 100 μM); (c) the common components in the reaction mixture required by both enzymes are cellobiose, calcium, and digitonin; (d) cellulose synthase has an essential requirement for magnesium (Ka = 0.89 mM); (e) cellulose synthase also requires a low concentration of calcium (Ka = 90 μM); (f) the optimal pH for cellulose synthase (7.6-8.0) is slightly higher than that for β-1,3-glucan synthase (7.2-7.6); (g) the Km for UGP-Glc for cotton (Gossypium hirsutum) cellulose synthase is 0.40 mM; (h) the Km for UDP-Glc for the β-1,3-glucan synthase is 0.43 mM.

IT 61693-23-6
RL: BIOL (Biological study)
(cellulose synthase of cotton fiber activation by cellobiose and)

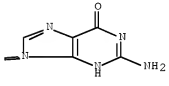
RN 61093-23-0 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

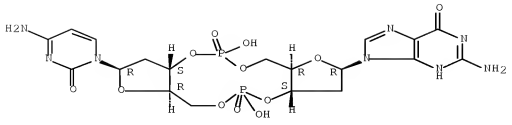


PAGE 1-B



L99 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:634347 CAPLUS Full-text
DOCUMENT NUMBER: 117:234347
TITLE: Quantitative evaluation of TOCSY data. Application to sugar ring conformational analysis
AUTHOR(S): Van Duynhoven, J. P. M.; Goudriaan, J.; Hilbers, C. W.; Wijmenga, S. S.
CORPORATE SOURCE: Nijmegen SON Res. Cent. Mol. Des. Struct. Synth., Natl. HF-NMR Facil., Nijmegen, 6525 ED, Neth.
SOURCE: Journal of the American Chemical Society (1992), 114(25), 10055-6
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Quant. structure information can be obtained from TOCSY spectra via the method of interactive back-calcn. of the cross peak intensities. The approach is demonstrated by the conformational anal. of the sugar rings in the cyclic dinucleotide cd(CpGp). The accuracy of the sugar conformational parameters obtained via this method is similar to the that obtained from J-coupling consts.
IT 129185-16-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(conformation of sugar ring in, NMR TOCSY in relation to)
RN 129185-16-6 CAPLUS
CN 3'-Guanylic acid, 2'-deoxycytidylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

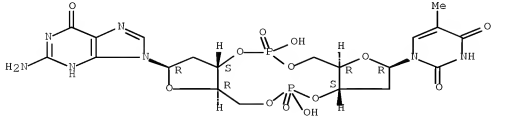


L99 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:444421 CAPLUS Full-text
DOCUMENT NUMBER: 117:44421
TITLE: HIV-1 DNA integration: mechanism of viral DNA cleavage and DNA strand transfer
AUTHOR(S): Engelman, Alan; Mizuuchi, Kiyoshi; Craigie, Robert
CORPORATE SOURCE: Lab. Mol. Biol., Natl. Inst. Diabetes Dig. Kidney Dis., Bethesda, MD, 20892, USA
SOURCE: Cell (Cambridge, MA, United States) (1991), 67(6), 1211-21
CODEN: CELLB5; ISSN: 0092-8674
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Retroviral DNA integration involves a coordinated set of DNA cutting and joining reactions. Linear viral DNA is cleaved as each 3' end to generate the precursor ends for integration. The resulting recessed 3' ends are inserted into target DNA by a subsequent DNA strand transfer reaction. Purified HIV-1 integration protein carries out both of these steps in vitro. Two novel forms of the dinucleotide cleaved from HIV-1 DNA were identified and 1, a cyclic dinucleotide, was used to analyze the stereochem. course of viral DNA cleavage. Both viral DNA cleavage and DNA strand transfer display inversion at chiral phosphorothioates during the course of the reaction. These results suggest that both reactions occur by a 1-step mechanism without involvement of a covalent protein-DNA intermediate.

IT 4568-15-4
RL: BIOL (Biological study)
(DNA cleavage product, of HIV virus, DNA integration in relation to)
RN 4568-15-4 CAPLUS
CN 3'-Guanylic acid, thymidylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L99 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1991:644592 CAPLUS Full-text

DOCUMENT NUMBER: 115:244592
TITLE: Chromonic lyomesophases formed by the self-assembly of the cyclic dinucleotide d(cGpGp)
AUTHOR(S): Bonazzi, Stefania; De Morais, Monica Miranda; Garbesi, Anna; Gottarelli, Giovanni; Mariani, Paolo; Spada, Gian Piero
CORPORATE SOURCE: Dip. Chim. Org. 'A Mangini", Univ. Bologna, Bologna, I-40127, Italy
SOURCE: Liquid Crystals (1991), 10(4), 495-506
CODEN: LICRE6; ISSN: 0267-8292
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The cyclic dinucleotide d(cGpGp) undergoes a self-association process in water to give, 1st, columnar aggregates similar to the 4-stranded helix of poly(G). Successively, at higher concentration, these aggregates self-organize to give a cholesteric and a hexagonal mesophase, the former of which appears only in biphasic systems. The self-assembly process in isotropic solution was studied by CD spectroscopy and the structure of the mesophases was investigated by optical microscopy and x-ray diffraction.

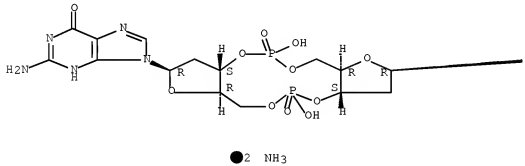
IT 137108-73-7
RL: PRP (Properties)
(liquid crystal, chromonic lyotropic phase formation in, by self-assembly)

RN 137108-73-7 CAPLUS

CN 3'-Guanylic acid, 2'-deoxyguanylyl-(3'→5')-2'-deoxy-, cyclic nucleotide, diammonium salt (9CI) (CA INDEX NAME)

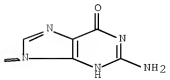
Absolute stereochemistry.

PAGE 1-A



2 NH_3

PAGE 1-B



L99 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1991:626890 CAPLUS Full-text

DOCUMENT NUMBER: 115:226890
TITLE: Cyclic diguanylic acid stimulates 1,4-β-glucan synthase from Saprolegnia monoica
AUTHOR(S): Girard, Vincent; Fevre, Michel; Mayer, Raphael; Benziman, Moshe
CORPORATE SOURCE: Cent. Genet. Mol. Cell., Univ. Lyon 1, Villeurbanne, 69622, Fr.
SOURCE: FEMS Microbiology Letters (1991), 82(3), 293-6
CODEN: FMLED7; ISSN: 0378-1097
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 1,4-β-Glucan synthase activity, but not 1,3-β-glucan-synthase activity, from S. monoica was stimulated by cyclic diguanylic acid, an immediate activator of Acetobacter xylinum cellulose synthase. This activator, which increased the Vmax without modifying the Km for UDP-glucose, was active on solubilized and partially purified enzymes. These results suggest that the fungal system shares a common regulatory mechanism with the bacterial system.

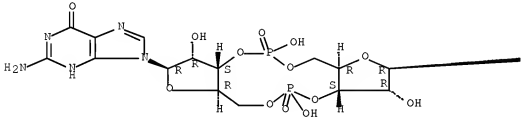
IT 61093-23-0
RL: BIOL (Biological study)
(glucan synthase of Saprolegnia monoica stimulation by)

RN 61093-23-0 CAPLUS

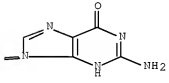
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L99 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1991:224003 CAPLUS Full-text
DOCUMENT NUMBER: 114:224003
TITLE: Oligomerization reactions of deoxyribonucleotides on montmorillonite clay: the effect of mononucleotide structure, phosphate activation and montmorillonite composition on phosphodiester bond formation
AUTHOR(S): Ferris, James P.; Kamaluddin; Ertem, Gozen

CORPORATE SOURCE: Rensselaer Polytech. Inst., Troy, NY, 12180-3590, USA
SOURCE: Origins of Life and Evolution of the Biosphere (1990), 20(3-4), 279-91
CODEN: OLEBEM; ISSN: 0169-6149
DOCUMENT TYPE: Journal
LANGUAGE: English

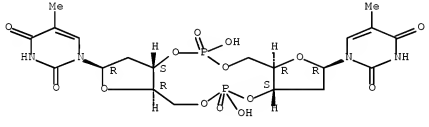
AB Both 2'-d-5'-GMP and 2'-d-5'-AMP bind 2 times more strongly to montmorillonite 22A than do 2'-d-5'-CMP and 5'-TMP. The dinucleotide d(pG)2 forms in 9.2% yield and the cyclic dinucleotide c(dpG)2 in 5.4% yield in the reaction of 2'-d-5'-GMP with 1-ethyl-3-(3- dimethylaminopropyl)carbodiimide (EDAC) in the presence of montmorillonite 22A. The yield of d(pC)2 (2.0%) is significantly lower but comparable to that obtained from 5'-TMP. The yield of dimers which contain the phosphodiester bond decreases as the reaction medium is changed from 0.2M NaCl to a mixture of 0.2M NaCl and 0.075M MgCl2. A low yield of d(pA)2 was observed in the condensation reaction of the imidazolide 5'-ImdpA on montmorillonite 22A. The cyclic nucleotide (3',5'-cdAMP) was obtained in 14% yield from 3'-ImdpA. The yield of d(pA)2 obtained when EDAC is used as the condensing agent increases with increasing iron content of the Na+-montmorillonite used as catalyst. Evidence is presented which shows that the acidity of Na+-montmorillonite is a necessary but not sufficient factor for montmorillonite catalysis of phosphodiester bond formation.

IT 25324-45-2P 60307-63-3P
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, in deoxyribonucleotides oligomerization on montmorillonite clay)

RN 25324-45-2 CAPLUS

CN 3'-Thymidylic acid, thymidylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

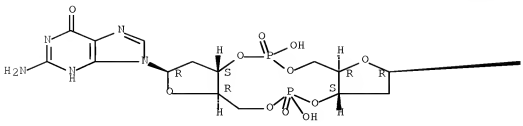


RN 60307-63-3 CAPLUS

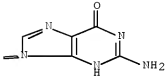
CN 3'-Guanylic acid, 2'-deoxyguanylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L99 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1991:97233 CAPLUS Full-text
DOCUMENT NUMBER: 114:97233
TITLE: The cyclic diguanylic acid regulatory system of cellulose synthesis in Acetobacter xylinum. Chemical synthesis and biological activity of cyclic nucleotide dimer, trimer, and phosphothioate derivatives
AUTHOR(S): Ross, Peter; Mayer, Raphael; Weinhouse, Haim; Amikam, Dorit; Huggirat, Yassir; Benziman, Moshe; De Vroom, Erik; Fidder, Alex; De Paus, Paul; et al.
CORPORATE SOURCE: Inst. Life Sci., Hebrew Univ., Jerusalem, 91904, Israel
SOURCE: Journal of Biological Chemistry (1990), 265(31), 18933-43
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An unusual compound, cyclic bis(3' → 5')diguanylic acid (c-di-GMP or cGpGp), regulates cellulose synthesis in Acetobacter xylinum. This cyclic dinucleotide acts as an allosteric, pos. effector of cellulose synthase (I) (Ka = 0.31 μM) and is inactivated via degradation by a Ca2+-sensitive cyclic nucleotide phosphodiesterase (II) (Km = 0.25 μM). A series of 13 analogs cyclic dimer and trimer nucleotides were synthesized, employing a phosphotriester approach, and tested for the ability to mimick cCpGp as activators of I and as substrates for II. Seven of the synthetic compds. stimulated I and all of these activators underwent the Ca2+-inhibited degradation reaction. The order of affinities for I activators was cGpGp .apprx. cdGpGp .apprx. cGp(S)Gp (S-diastereomer) > cIpGp > cdGpdGp > cXpGp > cIpIp > cGp(S)Gp (R-diastereomer). Three cyclic dinucleotides of negligible affinity for either enzyme were cApAp, cUpUp, and cCpCp. This same order of affinities essentially pertained to the analogs as inhibitors of II, but at least 1 cyclic dinucleotide, cXpXp, which did not bind to I, was also a substrate for degradation, demonstrating that although the 2 enzymes share a similar, high degree of specificity for c-diGMP, their cyclic dinucleotide binding sites are not identical. Phosphodiester bonds of activators in which

an exocyclic O atom was replaced with a S atom (cGp(S)Gp isomers) resisted the action of II, and such derivs. may be prototypes for synthetic nonhydrolyzable cGpGp analogs.

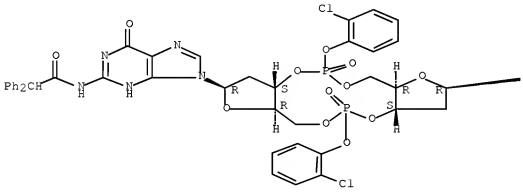
IT 129198-98-7P 132182-13-9P 132182-25-3P
132182-26-4P 132182-27-5P 132182-29-7P
132182-30-0P 132209-37-1P 132209-38-2P
132209-40-6P 132209-41-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection of)

RN 129198-98-7 CAPLUS

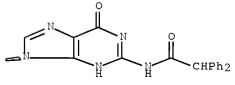
CN 3'-Guanylic acid, P-(2-chlorophenyl)-2'-deoxy-N-(diphenylacetyl)guanylyl-(3'→5')-2'-deoxy-N-(diphenylacetyl)-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

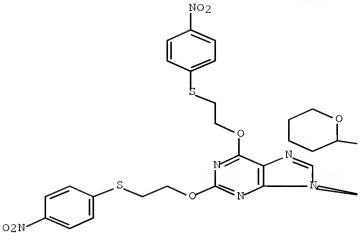


RN 132182-13-9 CAPLUS

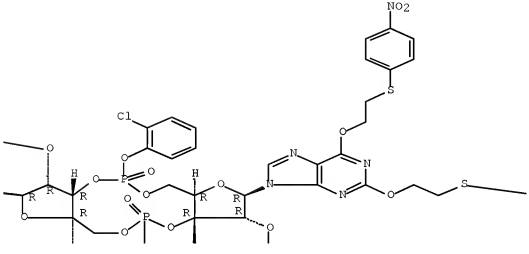
CN 3'-Xanthylic acid, P-(2-chlorophenyl)-2,6-bis-O-[2-[(4-nitrophenyl)thio]ethyl]-2'-O-(tetrahydro-2H-pyran-2-yl)xanthylyl-(3'→5')-2,6-bis-O-[2-[(4-nitrophenyl)thio]ethyl]-2'-O-(tetrahydro-2H-pyran-2-yl)-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

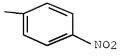
PAGE 1-A



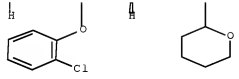
PAGE 1-B



PAGE 1-C



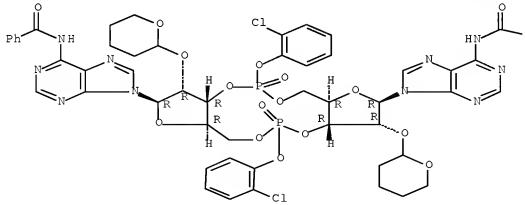
PAGE 2-B



RN 132182-25-3 CAPLUS
CN 3'-Adenylic acid, N-benzoyl-P-(2-chlorophenyl)-2'-O-(tetrahydro-2H-pyran-2-yl)adenylyl-(3'→5')-N-benzoyl-2'-O-(tetrahydro-2H-pyran-2-yl)-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



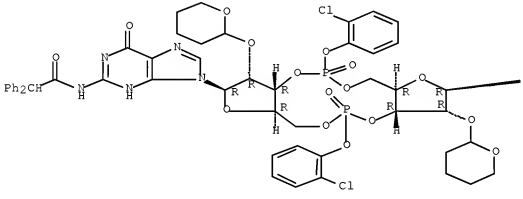
PAGE 1-B

Ph

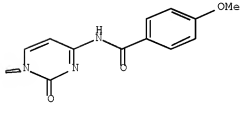
RN 132182-26-4 CAPLUS
CN 3'-Guanylic acid, P-(2-chlorophenyl)-N-(4-methoxybenzoyl)-2'-O-(tetrahydro-2H-pyran-2-yl)cytidylyl-(3'→5')-N-(diphenylacetyl)-2'-O-(tetrahydro-2H-pyran-2-yl)-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

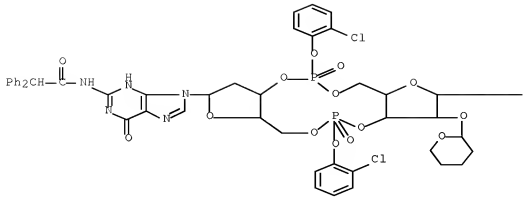


PAGE 1-B

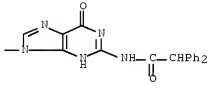


RN 132182-27-5 CAPLUS
CN 3'-Guanylic acid, P-(2-chlorophenyl)-2'-deoxy-N-(diphenylacetyl)guanylyl-(3'→5')-N-(diphenylacetyl)-2'-O-(tetrahydro-2H-pyran-2-yl)-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



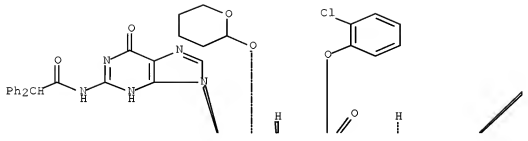
PAGE 1-B



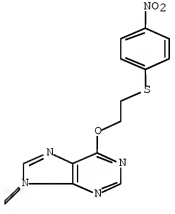
RN 132182-29-7 CAPLUS
CN 3'-Guanylic acid, P-(2-chlorophenyl)-6-O-[2-[(4-nitrophenyl)thio]ethyl]-2'-O-(tetrahydro-2H-pyran-2-yl)inosinylyl-(3'→5')-N-(diphenylacetyl)-2'-O-(tetrahydro-2H-pyran-2-yl)-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

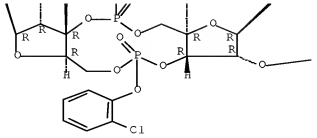
PAGE 1-A



PAGE 1-B



PAGE 2-A

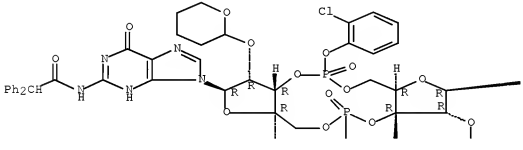


PAGE 2-B

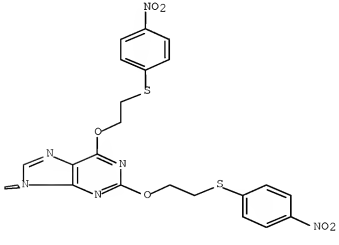
RN 132182-30-0 CAPLUS
CN 3'-Xanthylic acid, P-(2-chlorophenyl)-N-(diphenylacetyl)-2'-O-(tetrahydro-2H-pyran-2-yl)guanylyl-(3'→5')-2,6-bis-O-[2-[(4-nitrophenyl)thio]ethyl]-2'-O-(tetrahydro-2H-pyran-2-yl)-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

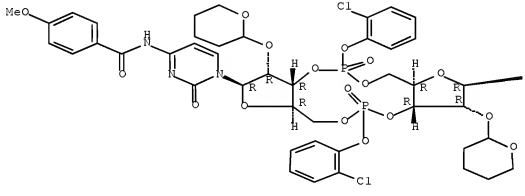


PAGE 2-A

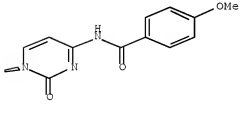
RN 132209-37-1 CAPLUS
CN 3'-Cytidylic acid, P-(2-chlorophenyl)-N-(4-methoxybenzoyl)-2'-O-(tetrahydro-2H-pyran-2-yl)cytidylyl-(3'→5')-N-(4-methoxybenzoyl)-2'-O-(tetrahydro-2H-pyran-2-yl)-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



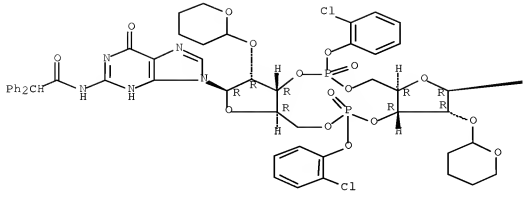
PAGE 1-B



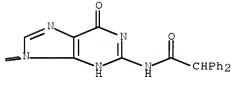
RN 132209-38-2 CAPLUS
CN 3'-Guanylic acid, P-(2-chlorophenyl)-N-(diphenylacetyl)-2'-O-(tetrahydro-2H-pyran-2-yl)guanylyl-(3'→5')-N-(diphenylacetyl)-2'-O-(tetrahydro-2H-pyran-2-yl)-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



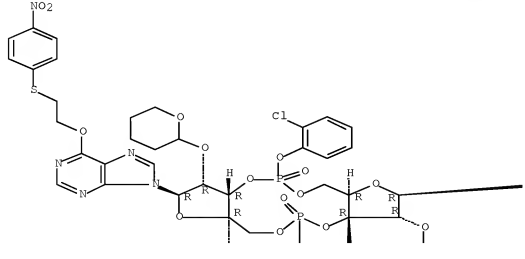
PAGE 1-B



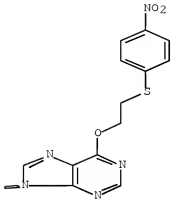
RN 132209-40-6 CAPLUS
CN 3'-Inosinic acid, P-(2-chlorophenyl)-6-O-[2-[(4-nitrophenyl)thio]ethyl]-2'-O-(tetrahydro-2H-pyran-2-yl)inosinylyl-(3'→5')-6-O-[2-[(4-nitrophenyl)thio]ethyl]-2'-O-(tetrahydro-2H-pyran-2-yl)-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

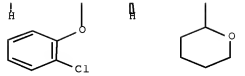
PAGE 1-A



PAGE 1-B

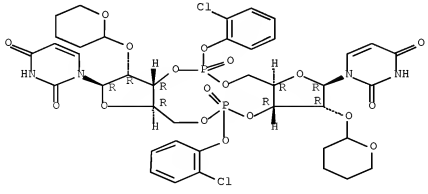


PAGE 2-A



RN 132209-41-7 CAPLUS
CN 3'-Uridylic acid, P-(2-chlorophenyl)-2'-O-(tetrahydro-2H-pyran-2-yl)uridylyl-(3'→5')-2'-O-(tetrahydro-2H-pyran-2-yl)-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



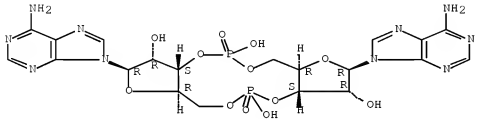
IT 54447-84-6P 60307-63-3P 61093-23-0P
73120-97-5P 73121-00-3P 79940-41-3P
132182-18-4P 132182-19-5P 132182-20-8P
132182-21-9P 132209-26-8P 132209-27-9P

132294-58-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with cellulose synthase and cyclic nucleotide phosphodiesterase of Acetobacter xylinum)

RN 54447-84-6 CAPLUS

CN 3'-Adenylic acid, adenylyl-(3'→5')-, cyclic nucleotide (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

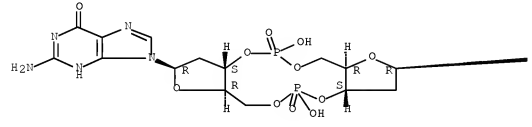


RN 60307-63-3 CAPLUS

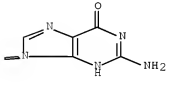
CN 3'-Guanylic acid, 2'-deoxyguanylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

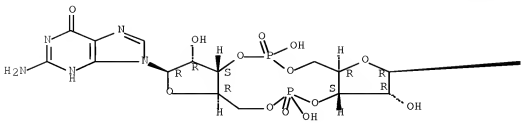


RN 61093-23-0 CAPLUS

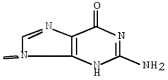
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



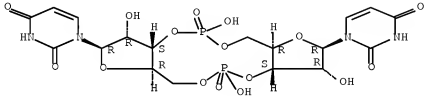
PAGE 1-B



RN 73120-97-5 CAPLUS

CN 3'-Uridylic acid, uridylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

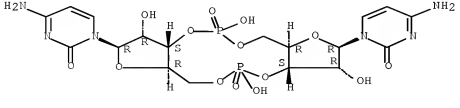
Absolute stereochemistry.



RN 73121-00-3 CAPLUS

CN 3'-Cytidylic acid, cytidylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

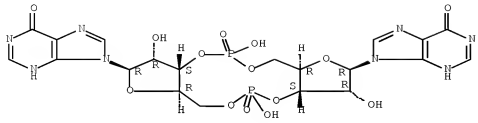
Absolute stereochemistry.



RN 79940-41-3 CAPLUS

CN 3'-Inosinic acid, inosinylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

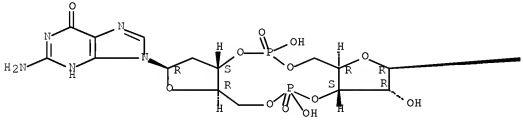
Absolute stereochemistry.



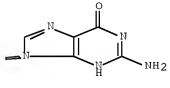
RN 132182-18-4 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



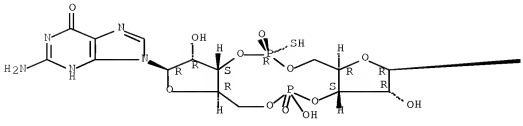
PAGE 1-B



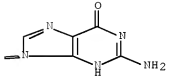
RN 132182-19-5 CAPLUS
CN 3'-Guanylic acid, [P(R)]-P-thioguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

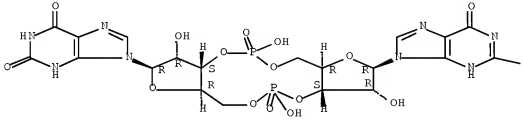


RN 132182-20-8 CAPLUS

CN 3'-Xanthylic acid, guanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

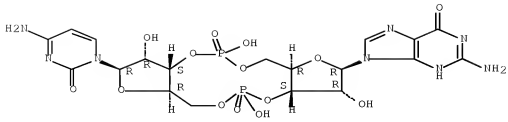


PAGE 1-B

RN 132182-21-9 CAPLUS

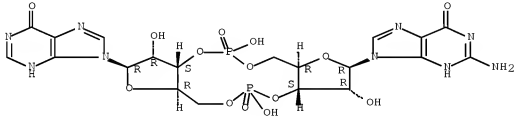
CN 3'-Guanylic acid, cytidylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 132209-26-8 CAPLUS
CN 3'-Guanylic acid, inosinylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

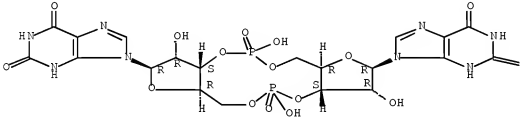
Absolute stereochemistry.



RN 132209-27-9 CAPLUS
CN 3'-Xanthylic acid, xanthylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



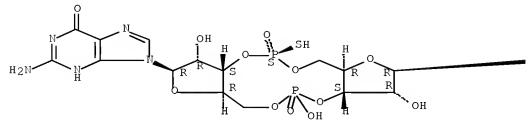
PAGE 1-B

RN 132294-58-7 CAPLUS

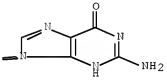
CN 3'-Guanylic acid, [P(S)]-P-thioguanylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L99 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:572629 CAPLUS Full-text
DOCUMENT NUMBER: 113:172629
TITLE: One pot solution synthesis of cyclic oligodeoxyribonucleotides
AUTHOR(S): Capobianco, Massimo; Carcuro, Antonio; Tondelli, Luisa; Garbesi, Anna; Bonora, Gian Maria
CORPORATE SOURCE: ICoCEA, CNR, Ozzano Emilia, I-40064, Italy
SOURCE: Nucleic Acids Research (1990), 18(9), 2661-9
CODEN: NARHAD; ISSN: 0305-1048
DOCUMENT TYPE: Journal
LANGUAGE: English

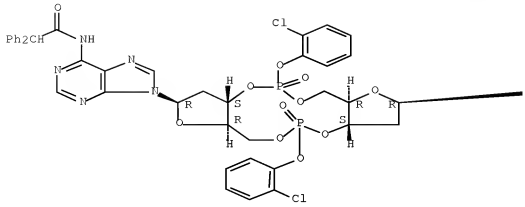
AB Several cyclic oligodeoxynucleotides with different base composition and size have been prepared from 5',3'-unprotected linear precursors, using a bifunctional phosphorylating reagent. The final deprotected oligomers have been characterized by 1H- and 31P-NMR. The present procedure is particularly useful for millimolar scale syntheses.

IT 119093-30-0P 119093-31-1P 129185-11-1P 129185-12-2P 129198-98-7P 129198-99-8P 129258-89-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection of)

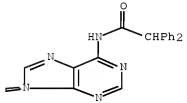
RN 119093-30-0 CAPLUS
CN 3'-Adenylic acid, P-(2-chlorophenyl)-2'-deoxy-N-(diphenylacetyl)adenylyl-(3'→5')-2'-deoxy-N-(diphenylacetyl)-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



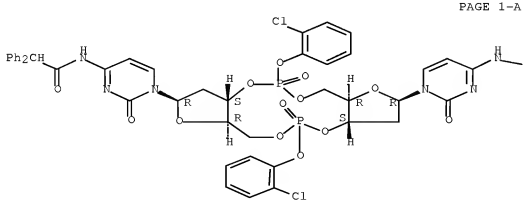
PAGE 1-B



RN 119093-31-1 CAPLUS
CN 3'-Cytidylic acid, P-(2-chlorophenyl)-2'-deoxy-N-(diphenylacetyl)cytidylyl-(3'→5')-2'-deoxy-N-(diphenylacetyl)-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

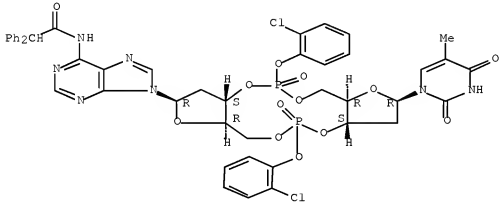
Absolute stereochemistry.

PAGE 1-A



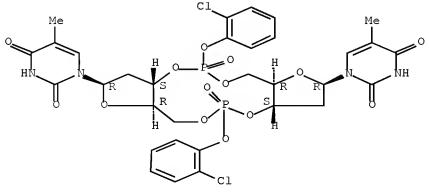
RN 129185-11-1 CAPLUS
CN 3'-Adenylic acid, P-(2-chlorophenyl)thymidylyl-(3'→5')-2'-deoxy-N-(diphenylacetyl)-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 129185-12-2 CAPLUS
CN 3'-Thymidylic acid, P-(chlorophenyl)thymidylyl-(3'→5')-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

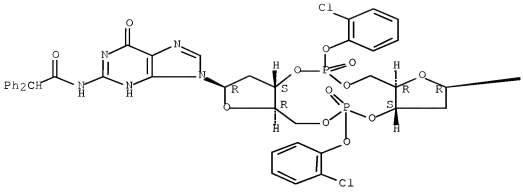
Absolute stereochemistry.



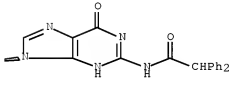
RN 129198-98-7 CAPLUS
CN 3'-Guanylic acid, P-(2-chlorophenyl)-2'-deoxy-N-(diphenylacetyl)guanylyl-(3'→5')-2'-deoxy-N-(diphenylacetyl)-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

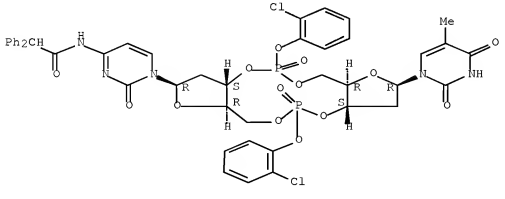


PAGE 1-B



RN 129198-99-8 CAPLUS
CN 3'-Thymidylic acid, P-(2-chlorophenyl)-2'-deoxy-N-(diphenylacetyl)cytidylyl-(3'→5')-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

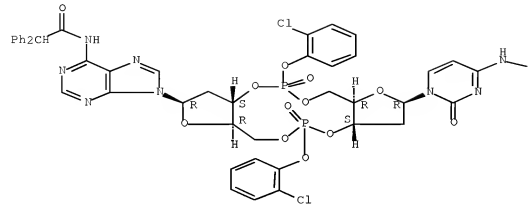
Absolute stereochemistry.



RN 129258-89-5 CAPLUS
CN 3'-Adenylic acid, P-(2-chlorophenyl)-2'-deoxy-N-(diphenylacetyl)cytidylyl-(3'→,5')-2'-deoxy-N-(diphenylacetyl)-, cyclic nucleotide, 2-chlorophenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

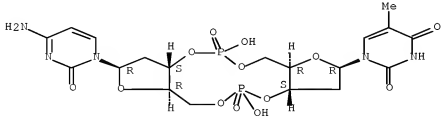
PAGE 1-A



PAGE 1-B

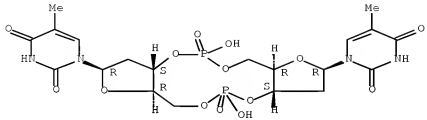
IT 4568-39-2P 25324-45-2P 60307-63-3P
79192-34-0P 109699-00-5P 129185-16-6P
129199-02-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 4568-39-2 CAPLUS
CN 3'-Thymidylic acid, 2'-deoxycytidylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 25324-45-2 CAPLUS
CN 3'-Thymidylic acid, thymidylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

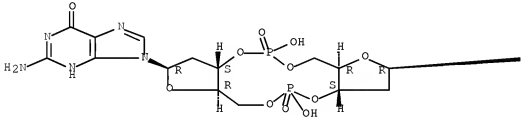
Absolute stereochemistry.



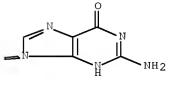
RN 60307-63-3 CAPLUS
CN 3'-Guanylic acid, 2'-deoxyguanylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

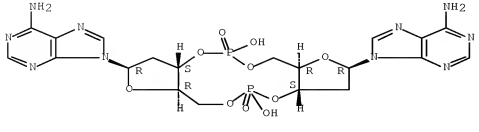


PAGE 1-B



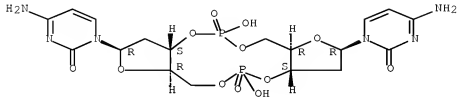
RN 79192-34-0 CAPLUS
CN 3'-Adenylic acid, 2'-deoxyadenylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



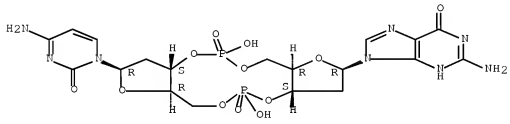
RN 109699-00-5 CAPLUS
CN 3'-Cytidylic acid, 2'-deoxycytidylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



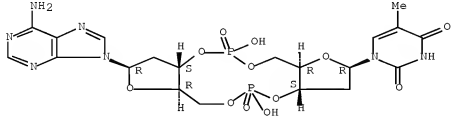
RN 129185-16-6 CAPLUS
CN 3'-Guanylic acid, 2'-deoxycytidylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 129199-02-6 CAPLUS
CN 3'-Adenylic acid, thymidylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

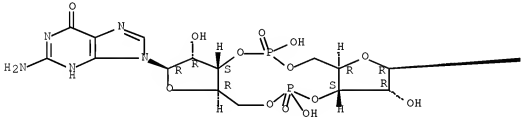


L99 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:547374 CAPLUS Full-text
DOCUMENT NUMBER: 113:147374
TITLE: Cyclic diguanylic acid behaves as a host molecule for planar intercalators
AUTHOR(S): Liaw, Yen Chywan; Gao, Yi Gui; Robinson, Howard;

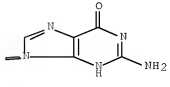
Sheldrick, George M.; Sliedregt, L. A. J. M.; Van der Marel, Gijs A.; Van Boom, Jacques H.; Wang, Andrew H. J.
CORPORATE SOURCE: Dep. Physiol. Biophys., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: FEBS Letters (1990), 264(2), 223-7
CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cyclic ribodiguanylic acid, c-(GpGp), is the endogenous effector regulator of cellulose synthase. Its 3-dimensional structure from 2 different crystal forms (tetragonal and trigonal) has been determined by x-ray diffraction anal. at 1-Å resolution In both crystal forms, 2 independent c-(GpGp) mols. associate with each other to form a self-intercalated dimer. A hydrated Co ion is found to coordinate to 2 N7 atoms of adjacent guanines, forcing these 2 guanines to destack with a large dihedral angle (32°), in the dimer of the tetragonal form. This metal coordination mechanism may be relevant to that of the anticancer drug cisplatin. Moreover, c-(GpGp) exhibits unusual spectral properties not seen in any other cyclic dinucleotide. It interacts with planar organic intercalator mols. in ways similar to double helical DNA. A cagelike model is proposed consisting of a tetrameric c-(GpGp) aggregate in which a large cavity (host) is generated to afford a binding site for certain planar intercalators (guests).
IT 61093-23-0D, cobalt complexes
RL: PRP (Properties)
(crystal structure of, ion coordination and intercalation properties in relation to)
RN 61093-23-0 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L99 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:454867 CAPLUS Full-text
DOCUMENT NUMBER: 113:54867

TITLE: Atomic-resolution structure of the cellulose synthase regulator cyclic diguanylic acid

AUTHOR(S): Egli, Martin; Gessner, Reinhard V.; Williams, Loren Dean; Quigley, Gary J.; Van der Marel, Gijs A.; Van Boom, Jacques H.; Rich, Alexander; Frederick, Christine A.

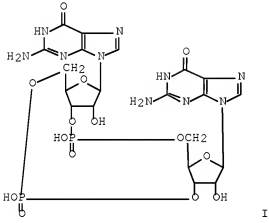
CORPORATE SOURCE: Dep. Biol., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1990), 87(8), 3235-9
CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB The x-ray crystal structure of cyclic diguanylic acid at atomic resolution is reported. The structure contains 2 independent mols. that adopt almost identical conformations. The two mols. form self-intercalated units that are stacked on each other. Two different G·G base-pairing modes occur between the stacks. The more stable one has 2 or possibly 3 H bonds between 2 guanines and is related to the type of H bonding that is believed to exist between G-rich strands at the ends of chromosomes.

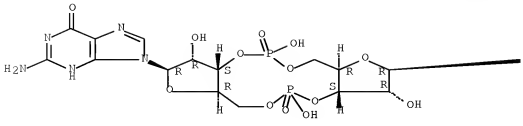
IT 61093-23-0
RL: PRP (Properties)
(crystal structure of)

RN 61093-23-0 CAPLUS

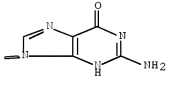
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



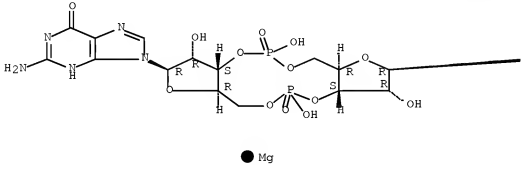
PAGE 1-B



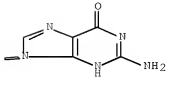
IT 128235-44-9
RL: PRP (Properties)
(structure of)
RN 128235-44-9 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic nucleotide, magnesium salt (1:1) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



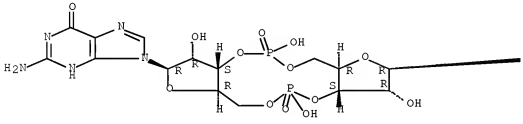
L99 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:51881 CAPLUS Full-text
DOCUMENT NUMBER: 112:51881
TITLE: Cyclic diguanylic acid and cellulose synthesis in Agrobacterium tumefaciens
AUTHOR(S): Amikam, Dorit; Benziman, Moshe
CORPORATE SOURCE: Inst. Life Sci., Hebrew Univ., Jerusalem, 91904, Israel
SOURCE: Journal of Bacteriology (1989), 171(12), 6649-55
CODEN: JOBAAY; ISSN: 0021-9193
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The occurrence of the novel regulatory nucleotide bis(3',5')-cyclic diguanylic acid (I) and its relation to cellulose biogenesis in the plant pathogen A. tumefaciens was studied. I was detected in acid exts. of 32P-labeled cells grown in various media, and an enzyme responsible for its formation from GTP was found in cell-free prepns. Cellulose synthesis in vivo was quant. assessed with [14C]glucose as a tracer. The organism produced cellulose during growth in the absence of plant cells, and this capacity was retained in resting cells. Synthesis of a cellulosic product from UDPglucose in vitro with membrane prepns. was markedly stimulated by I and its precursor GTP and was further enhanced by Ca. The Ca effect was attributed to inhibition of a I-degrading enzyme shown to be present in the cellulose synthase-containing membranes.

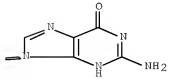
IT 61093-23-0
RL: BIOL (Biological study)
(of Agrobacterium tumefaciens, cellulose formation in relation to)
RN 61093-23-0 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L99 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1987:116265 CAPLUS Full-text
DOCUMENT NUMBER: 106:116265
ORIGINAL REFERENCE NO.: 106:18945a,18948a
TITLE: Regulation of cellulose synthesis in Acetobacter xylinum by cyclic diguanylic acid
AUTHOR(S): Ross, P.; Weinhouse, H.; Aloni, Y.; Michaeli, D.; Weinberger-Ohana, P.; Mayer, R.; Braun, S.; De Vroom, E.; Van der Marel, G. A.; et al.
CORPORATE SOURCE: Inst. Life Sci., Hebrew Univ. Jerusalem, Jerusalem, 91904, Israel
SOURCE: Nature (London, United Kingdom) (1987), 325(6101), 279-81
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A model system to study the mechanism of cellulose biogenesis is the bacterium A. xylinum which produces pure cellulose as an extracellular product. It was from this organism that in vitro prepns. which possessed high levels of cellulose synthase activity were first obtained in both membranous and soluble forms. This activity is subject to a complex multi-component regulatory system, in which the synthase is directly affected by an unusual cyclic nucleotide activator enzymically formed from GTP, and indirectly by a Ca2+-sensitive phosphodiesterase which degrades the activator. The cellulose synthase activator has now been identified as bis-(3'→5')-cyclic diguanylic acid on the basis of mass spectroscopic data, NMR anal. and comparison with chemical synthesized material. Intermediary steps in the synthesis and degradation of this novel circular dinucleotide are reported, the steps are integrated into a model for the regulation of cellulose synthesis.

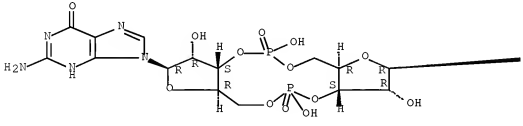
IT 61093-23-0
RL: BIOL (Biological study)
(cellulose formation in Acetobacter xylinum regulation by)

RN 61093-23-0 CAPLUS

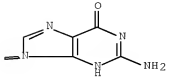
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L99 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1981:599624 CAPLUS Full-text
DOCUMENT NUMBER: 95:199624
ORIGINAL REFERENCE NO.: 95:33281a,33284a
TITLE: Functional analysis of influenza RNA polymerase activity by the use of caps, oligonucleotides and polynucleotides
AUTHOR(S): Stridh, S.; Oeberg, B.; Chattopadhyaya, J.; Josephson, S.
CORPORATE SOURCE: Dep. Antiviral Chemother. Res., Astra Laakemedel AB, Soedertaelje, Swed.
SOURCE: Antiviral Research (1981), 1(2), 97-105
CODEN: ARSRDR; ISSN: 0166-3542
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of caps, dinucleotides, oligonucleotides, and polynucleotides on influenza virus RNA polymerase activity was investigated. Both Me groups in a cap are necessary for optimal stimulation of polymerase activity. Both m7G(5')ppp(5')Am (where m7G is 7-methylguanosine and Am is 2-O-methyladenosine) and ApG stimulated the influenza RNA polymerase activity and seemed to interact at different sites. Of the 16 homopolynucleotides tested, 7 inhibited influenza RNA polymerase by 50% at 2-10 μg/mL. Poly(G) gave a 90% reduction of influenza virus plaque formation at 10 μg/mL. An oligodeoxyribonucleotide complementary to the 12 terminal nucleotides of the 3' end of influenza virus RNA was synthesized. This oligonucleotide did not selectively inhibit influenza RNA polymerase.

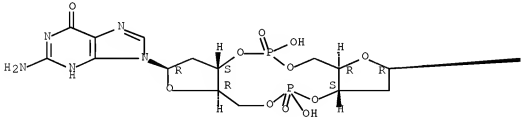
IT 60307-63-3 79192-34-0
RL: BIOL (Biological study)
(RNA polymerase of influenza virus response to, mol. mechanism in relation to)

RN 60307-63-3 CAPLUS

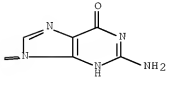
CN 3'-Guanylic acid, 2'-deoxyguanylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

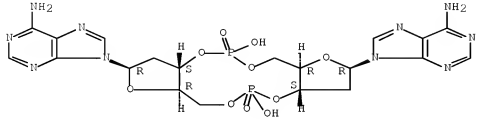


PAGE 1-B



RN 79192-34-0 CAPLUS
CN 3'-Adenylic acid, 2'-deoxyadenylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

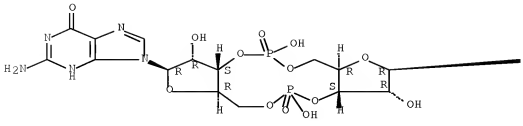
Absolute stereochemistry.



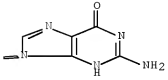
L99 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1980:210354 CAPLUS Full-text
DOCUMENT NUMBER: 92:210354
ORIGINAL REFERENCE NO.: 92:34007a,34010a
TITLE: Studies on transfer ribonucleic acids and related compounds. XXVI. Circular dichroic properties of cyclic oligoribonucleotides and their linear counterparts
AUTHOR(S): Markham, A. F.; Nakagawa, E.; Ohtsuka, E.; Ikehara, M.
CORPORATE SOURCE: Fac. Pharm. Sci., Osaka Univ., Suita, 565, Japan
SOURCE: Biopolymers (1980), 19(2), 285-96
CODEN: BIPMAA; ISSN: 0006-3525
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The CD spectra of cUpUp, cCpCp, and cGpGp (c preceding an oligonucleotide indicates a 3',5'-phosphodiester linkage, e.g., cyclic dicytidylic acid) derived from DCC-catalyzed polymerization of the relevant protected ribonucleoside 3'-phosphates are described. Similar studies on UMP, uridine 2',3'-cyclic phosphate, and uridine 3',5'-cyclic phosphate, as well as c(UpUpUp) and c(UpUpUpUp), are presented. The spectral properties of the cyclic oligomers were compared with those of the corresponding linear oligomers with terminal 3'-phosphates to demonstrate that disruption of normal right-handed base stacking is considerable in these RNA loops.
IT 61093-23-0 73120-97-5 73121-00-3
RL: PRP (Properties)
(CD of)
RN 61093-23-0 CAPLUS
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



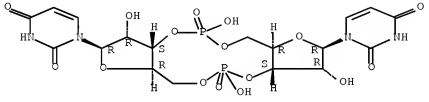
PAGE 1-B



RN 73120-97-5 CAPLUS

CN 3'-Uridylic acid, uridylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

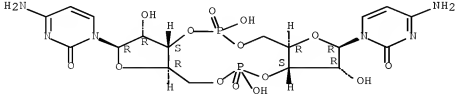
Absolute stereochemistry.



RN 73121-00-3 CAPLUS

CN 3'-Cytidylic acid, cytidylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L99 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1980:164219 CAPLUS Full-text
DOCUMENT NUMBER: 92:164219

ORIGINAL REFERENCE NO.: 92:26633a,26636a
TITLE: Studies on transfer ribonucleic acids and related compounds. XXVII. Linear and cyclic oligonucleotides obtained by polymerization of protected ribonucleoside 3'-phosphates
AUTHOR(S): Markham, Alexander F.; Nakagawa, Eiko; Ohtsuka, Eiko; Ikehara, Morio
CORPORATE SOURCE: Fac. Pharm. Sci., Osaka Univ., Suita, 565, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1979), 27(12), 2988-96
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English

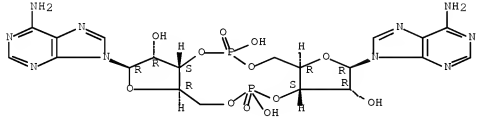
AB An improved method for the dicyclohexylcarbodiimide-catalyzed polymerization of protected ribonucleoside 3'-phosphates (cytidine, adenosine, uridine, and guanosine 3'-phosphates) was described. The formation of 5'-O-pyridinium compds. was eliminated, and various 5'-O-monomethoxytritylated could be rapidly isolated in reasonable yields. The isolation and purification of 3',5'-cyclized oligonucleotides [cCpCp, cUp(Up)n, or cGpGp] was described.

IT 54447-84-6P 58432-29-4P 61093-23-0P 73120-97-5P 73121-00-3P 73253-11-4P 73362-99-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 54447-84-6 CAPLUS

CN 3'-Adenylic acid, adenylyl-(3'→5')-, cyclic nucleotide (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

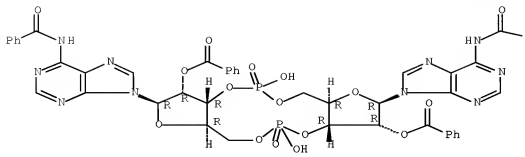


RN 58432-29-4 CAPLUS

CN 3'-Adenylic acid, N-benzoyl-2'-O-benzoyladenylyl-(3'→5')-N-benzoyl-, 2'-benzoate, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



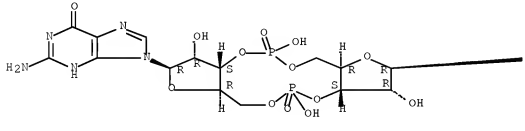
PAGE 1-B

RN 61093-23-0 CAPLUS

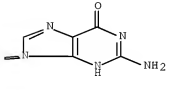
CN 3'-Guanylic acid, guanylyl-(3'→5')-, cyclic 3'→5'''-nucleotide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



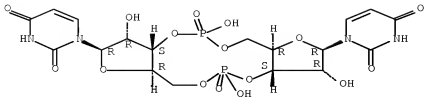
PAGE 1-B



RN 73120-97-5 CAPLUS

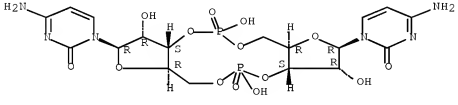
CN 3'-Uridylic acid, uridylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 73121-00-3 CAPLUS
CN 3'-Cytidylic acid, cytidylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

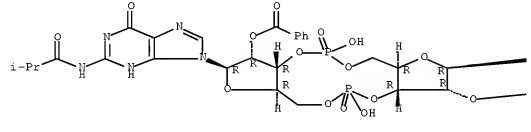
Absolute stereochemistry.



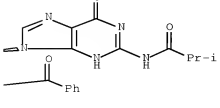
RN 73353-11-4 CAPLUS
CN 3'-Guanylic acid, 2'-O-benzoyl-N-(2-methyl-1-oxopropyl)guanylyl-(3'→5')-N-(2-methyl-1-oxopropyl)-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

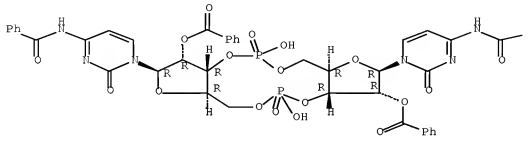


RN 73362-99-9 CAPLUS

CN 3'-Cytidylic acid, N-benzoyl-2'-O-benzoylcytidylyl-(3'→5')-N-benzoyl-, cyclic nucleotide, 2'-benzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

L99 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1976:458772 CAPLUS Full-text
DOCUMENT NUMBER: 85:58772
ORIGINAL REFERENCE NO.: 85:9483a,9486a
TITLE: Subsite interactions of ribonuclease T1: binding studies of dimeric substrate analogs
AUTHOR(S): Walz, Frederick G., Jr.; Terenna, Barry
CORPORATE SOURCE: Dep. Biol. Sci., State Univ. New York, Albany, NY, USA
SOURCE: Biochemistry (1976), 15(13), 2837-42
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

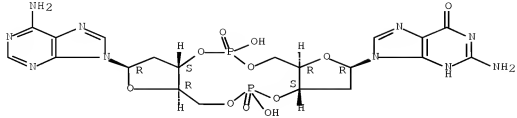
AB Uv difference spectral binding studies of RNase T1 (I) with pGp, ApG, CpG, UpG, dGpdA, dGpdC, dGpdG, dGpdT, dTpdG, pdApdG, pdTpdG, pdGpdA, pdGpdG, pdGpdT, cyclic (pdGpdA), and cyclic (pdGpdG) were conducted at pH 5.0, 0.2M ionic strength and 25°. Under these conditions, the characteristic difference spectrum and association constant for (1:1) I binding were determined for each ligand. The binding of guanosine- and deoxyguanosine-containing ligands could be distinguished by the shapes of their difference spectra. The results indicated that the guanine moiety of each ligand was bound at I's primary recognition site. Evidence of a specific I subsite for binding the adenine moiety of ApG and pdApdG is presented. The proposal made elsewhere of a specific I subsite for binding the 5'-phosphate group of a complexed guanosine moiety is not supported by this data. Preliminary evidence for the existence of 2 addnl. I subsites and the effect of oligomer conformation on I binding are also discussed.

IT 4568-41-6 60307-63-3
RL: PROC (Process)
(RNase T1 binding of)

RN 4568-41-6 CAPLUS

CN 3'-Guanylic acid, 2'-deoxyadenylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

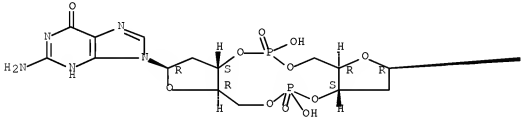
Absolute stereochemistry.



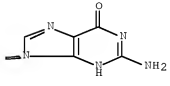
RN 60307-63-3 CAPLUS
CN 3'-Guanylic acid, 2'-deoxyguanylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L99 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1965:431957 CAPLUS Full-text
DOCUMENT NUMBER: 63:31957
ORIGINAL REFERENCE NO.: 63:5723f-h
TITLE: Polynucleotides. XLIV. The synthesis of dodecanucleotides containing the repeating trinucleotide sequence thymidylyl-(3' → 5')-thymidylyl-(3' → 5')deoxycytidine
AUTHOR(S): Jacob, T. M.; Khorana, H. G.
CORPORATE SOURCE: Univ. of Wisconsin, Madison
SOURCE: Journal of the American Chemical Society (1965), 87(13), 2971-81
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English

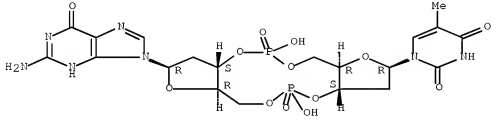
AB The synthesis of the dodecanucleotide containing the repeating trinucleotide sequence thymidylyl-(3' → 5')-thymidylyl-(3' → 5')-deoxycytidine (d-TpTpCpTpTpCpTpTpCpTpTpC) has been accomplished. The synthetic approach used involved the stepwise condensation of a suitably protected mononucleotide to the 3'-hydroxyl end of a growing oligonucleotide chain. The starting materials were 5'-O-tritylthymidine and the protected mononucleotides N-anisoyl-3'-O-acetyldeoxycytidine 5'-phosphate and 3'-O-acetylthymidine 5'-phosphate. The condensing agents used were dicyclohexylcarbodiimide or mesitylenesulfonyl chloride. After each condensation step, the terminal 3'-O-acetyl group was selectively removed from the protected oligo- or polynucleotides by a mildly alkaline treatment, and the latter products were purified by chromatog. on DEAE-cellulose anion-exchanger columns. By using an increasing excess of the protected mononucleotide with an increase in the chain length of the oligonucleotide, high yields (70-80%) with respect to the latter component could be maintained. All of the intermediate oligo- and polynucleotides, protected and unprotected, have been isolated pure and characterized.

IT 4568-15-4P, Guanosine, 5'-O-phosphorylthymidylyl-(3' → 5')-2'-deoxy-, cyclic nucleotide 4568-39-2P, Thymidine, 2'-deoxycytidylyl-(5'→3')-, 5'-phosphate, cyclic nucleotide 4568-41-6P, Guanosine, 2'-deoxy-5'-O-phosphoryl-adenylyl-(3'→5')-2'-deoxy-, cyclic nucleotide 4568-42-7P, Adenosine, 2'-deoxy-5'-O-phosphorylcytidylyl-(3'→5')-2'-deoxy-, cyclic nucleotide
RL: PREP (Preparation)
(preparation of)

RN 4568-15-4 CAPLUS

CN 3'-Guanylic acid, thymidylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

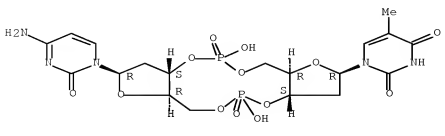
Absolute stereochemistry.



RN 4568-39-2 CAPLUS

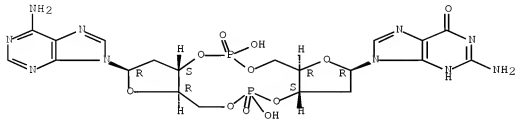
CN 3'-Thymidylic acid, 2'-deoxycytidylyl-(3'→5')-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



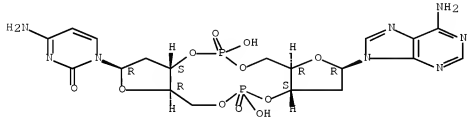
RN 4568-41-6 CAPLUS
CN 3'-Guanylic acid, 2'-deoxyadenylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 4568-42-7 CAPLUS
CN 3'-Adenylic acid, 2'-deoxycytidylyl-(3'→5')-2'-deoxy-, cyclic nucleotide (9CI) (CA INDEX NAME)

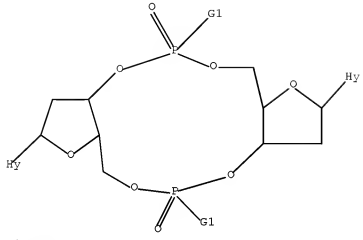
Absolute stereochemistry.



FILE 'HOME' ENTERED AT 15:43:12 ON 19 MAR 2008

SEARCH HISTORY

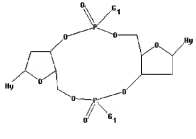
```
=> d stat que l86; d his nofile
L8                STR
```

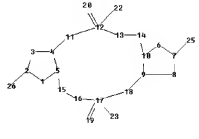


G1 O,S,Se

Structure attributes must be viewed using STN Express query preparation.

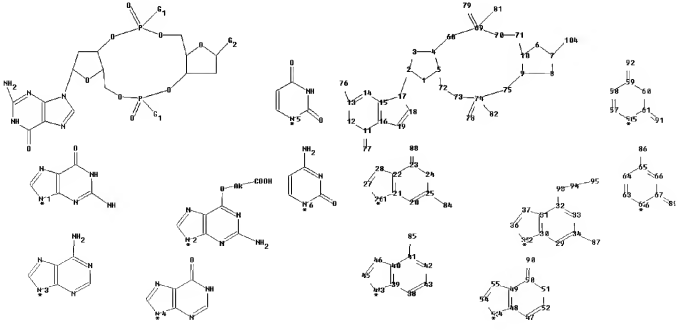
Uploading L8.str






```
chain nodes :
19  20  22  23  25  26
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  17  18
chain bonds :
2-26  7-25  12-20  12-22  17-19  17-23
ring bonds :
1-2  1-5  2-3  3-4  4-5  4-11  5-15  6-7  6-10  7-8  8-9  9-10  9-18  10-14  11-12
```

```
12-13  13-14  15-16  16-17  17-18
exact/norm bonds :
1-2  1-5  2-3  2-26  3-4  4-5  4-11  5-15  6-7  6-10  7-8  7-25  8-9  9-10  9-18
10-14  11-12  12-13  12-20  12-22  13-14  15-16  16-17  17-18  17-19  17-23


G1:O,S,Se

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:CLASS
20:CLASS  22:CLASS  23:CLASS  25:CLASS  26:Atom
Generic attributes :
25:
Saturation              : Unsaturated
26:
Saturation              : Unsaturated

Element Count :
Node 25: Limited
    N,N2

Node 26: Limited
    N,N2




L13          136 SEA FILE=REGISTRY SSS FUL L8
L83              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

Uploading L83.str
```



```
chain nodes :
76  77  78  79  81  82  84  85  86  87  88  89  90  91  92  93  94  95  104
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  17  18  19  20  21  22  23
24  25  26  27  28  29  30  31  32  33  34  35  36  37  38  39  40  41  42  43  44
45  46  47  48  49  50  51  52  53  54  55  56  57  58  59  60  61  62  63  64  65
66  67  68  69  70  71  72  73  74  75
chain bonds :
2-17  7-104  11-77  13-76  23-88  25-84  32-93  34-87  41-85  50-90  59-92  61-91
65-86  67-89  69-79  69-81  74-78  74-82  93-94  94-95
ring bonds :
1-2  1-5  2-3  3-4  4-5  4-68  5-72  6-7  6-10  7-8  8-9  9-10  9-75  10-71  11-12
11-16  12-13  13-14  14-15  15-16  15-17  16-19  17-18  18-19  20-21  20-25  21-22
21-26  22-23  22-28  23-24  24-25  26-27  27-28  29-30  29-34  30-31  30-35  31-32
31-37  32-33  33-34  35-36  36-37  38-39  38-43  39-40  39-44  40-41  40-46  41-42
42-43  44-45  45-46  47-48  47-52  48-49  48-53  49-50  49-55  50-51  51-52  53-54
54-55  56-57  56-61  57-58  58-59  59-60  60-61  62-63  62-67  63-64  64-65  65-66
66-67  68-69  69-70  70-71  72-73  73-74  74-75
exact/norm bonds :
1-2  1-5  2-3  2-17  3-4  4-5  4-68  5-72  6-7  6-10  7-8  7-104  8-9  9-10  9-75
10-71  11-12  11-16  11-77  12-13  13-14  13-76  14-15  15-16  15-17  16-19  17-18
18-19  20-21  20-25  21-22  21-26  22-23  22-28  23-24  23-88  24-25  25-84  26-27
27-28  30-35  31-37  32-93  34-87  35-36  36-37  39-44  40-46  41-85  44-45  45-46
47-48  47-52  48-49  48-53  49-50  49-55  50-51  50-90  51-52  53-54  54-55  56-57
56-61  57-58  58-59  59-60  59-92  60-61  61-91  62-63  62-67  63-64  64-65  65-66
65-86  66-67  67-89  68-69  69-70  69-79  69-81  70-71  72-73  73-74  74-75  74-78
74-82  93-94  94-95
normalized bonds :
29-30  29-34  30-31  31-32  32-33  33-34  38-39  38-43  39-40  40-41  41-42  42-43


G1:O,S,Se

G2:[*1],[*2],[*3],[*4],[*5],[*6]

Connectivity :
94:2 E exact RC ring/chain
Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:Atom
20:Atom  21:Atom  22:Atom  23:Atom  24:Atom  25:Atom  26:Atom  27:Atom  28:Atom
29:Atom  30:Atom  31:Atom  32:Atom  33:Atom  34:Atom  35:Atom  36:Atom  37:Atom
38:Atom  39:Atom  40:Atom  41:Atom  42:Atom  43:Atom  44:Atom  45:Atom  46:Atom
47:Atom  48:Atom  49:Atom  50:Atom  51:Atom  52:Atom  53:Atom  54:Atom  55:Atom
56:Atom  57:Atom  58:Atom  59:Atom  60:Atom  61:Atom  62:Atom  63:Atom  64:Atom
65:Atom  66:Atom  67:Atom  68:Atom  69:Atom  70:Atom  71:Atom  72:Atom  73:Atom
74:Atom  75:Atom  76:CLASS  77:CLASS  78:CLASS  79:CLASS  81:CLASS  82:CLASS
84:CLASS  85:CLASS  86:CLASS  87:CLASS  88:CLASS  89:CLASS  90:CLASS  91:CLASS
92:CLASS  93:CLASS  94:CLASS  95:CLASS  104:CLASS



L86          40 SEA FILE=REGISTRY SUB=L13 SSS FUL L83

100.0% PROCESSED      58 ITERATIONS                          40 ANSWERS
SEARCH TIME: 00.00.01
```

```
     (FILE 'HOME' ENTERED AT 13:55:35 ON 19 MAR 2008)

     FILE 'CAPLUS' ENTERED AT 13:55:47 ON 19 MAR 2008
                  E US2006-565591/APPS
L1             1 SEA ABB=ON  US2006-565591/AP
                  D SCAN
                  SEL RN

     FILE 'REGISTRY' ENTERED AT 13:56:21 ON 19 MAR 2008
L2            31 SEA ABB=ON  (132182-18-4/BI OR 132182-19-5/BI OR 132182-21-9/BI
                   OR 132209-26-8/BI OR 132294-58-7/BI OR 232933-52-7/BI OR
                  3353-33-1/BI OR 60307-63-3/BI OR 61093-23-0/BI OR 849214-01-3/B
                  I OR 849214-02-4/BI OR 849214-03-5/BI OR 849214-04-6/BI OR
                  849214-05-7/BI OR 849214-06-8/BI OR 849214-07-9/BI OR 849214-08
                  -0/BI OR 849214-09-1/BI OR 849214-10-4/BI OR 849214-11-5/BI OR
                  849214-12-6/BI OR 849214-13-7/BI OR 849214-14-8/BI OR 849214-15
                  -9/BI OR 849214-16-0/BI OR 849447-99-0/BI OR 849448-00-6/BI OR
                  849448-01-7/BI OR 849448-02-8/BI OR 849448-03-9/BI OR 9012-56-0
                  /BI)
                  D SCAN
L3                STRUCTURE UPLOADED
L4             3 SEA SSS SAM L3
                  D SCAN
L5             2 SEA ABB=ON  L4 AND L2

     FILE 'ZCAPLUS' ENTERED AT 14:17:46 ON 19 MAR 2008
L6             1 SEA ABB=ON  L4
                  D SCAN TI
L7                STRUCTURE UPLOADED
                  D L7

     FILE 'REGISTRY' ENTERED AT 14:22:09 ON 19 MAR 2008
L8                STRUCTURE UPLOADED
                  D
L9            12 SEA SSS SAM L8
L10            9 SEA ABB=ON  L9 NOT L4
                  D SCAN

     FILE 'ZCAPLUS' ENTERED AT 14:24:00 ON 19 MAR 2008
L11           10 SEA ABB=ON  L10

     FILE 'REGISTRY' ENTERED AT 14:24:13 ON 19 MAR 2008
L12         1696 SEA SSS FUL L8 EXTEND
L13          136 SEA SSS FUL L8
                  SAVE TEMP L13 ARC591FULL/A

     FILE 'CAPLUS' ENTERED AT 14:24:50 ON 19 MAR 2008
L14          149 SEA ABB=ON  L13
L15           36 SEA ABB=ON  KARAOLIS D?/AU
L16            9 SEA ABB=ON  (L1 OR L15) AND L14
                  D SCAN L1
                  D SCAN L1

     FILE 'STNGUIDE' ENTERED AT 14:32:59 ON 19 MAR 2008

     FILE 'CAPLUS' ENTERED AT 14:36:01 ON 19 MAR 2008
                  E "BIOFILMS (MICROBIAL)"+ALL/CT
```

```
                E "VIRULENCE (MICROBIAL)"+ALL/CT
L17        33297 SEA ABB=ON  STAPHYLOCOCCUS AUREUS/CT
L18         3744 SEA ABB=ON  VIBRIO CHOLERAE/CT
L19         2146 SEA ABB=ON  SALMONELLA ENTERITIDIS/CT
L20        80199 SEA ABB=ON  INFECTION/CT
L21         2738 SEA ABB=ON  MASTITIS/CT
L22        50328 SEA ABB=ON  ANTIBACTERIAL AGENTS/CT
                E MICROBES/CT
                E ANTIMICROBIAL/CT
L23         4983 SEA ABB=ON  COLONIZ?/OBI
L24        22200 SEA ABB=ON  ANTIMICROBIAL AGENTS/CT
L25         8625 SEA ABB=ON  MICROBE#/OBI
L26       340478 SEA ABB=ON  MICROBIAL/OBI
L27        25812 SEA ABB=ON  VIRULENCE/CW
L28        13036 SEA ABB=ON  BIOFILM#/OBI
L29           47 SEA ABB=ON  L14 AND (L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR
                             L23 OR L24 OR L25 OR L26 OR L27 OR L28)
L30           70 SEA ABB=ON  L14 AND (PY<2004 OR AY<2004 OR PRY<2004)
L31            3 SEA ABB=ON  L30 AND (L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR
                             L23 OR L24 OR L25 OR L26 OR L27 OR L28)
L32       394845 SEA ABB=ON  BACTERI?/OBI
L33            5 SEA ABB=ON  L30 AND (L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR
                             L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L32)
                D SCAN
L34           15 SEA ABB=ON  L14(L)(THU OR BAC OR PAC OR PKT OR DMA)/RL
L35            6 SEA ABB=ON  L34 AND L30
L36      2343963 SEA ABB=ON  PHARMAC?/SC,SX
L37            4 SEA ABB=ON  L30 AND L36
L38       122405 SEA ABB=ON  IMPLANT?/OBI
L39        51350 SEA ABB=ON  PROSTHE?/OBI
L40       222938 SEA ABB=ON  DRUG DELIVERY SYSTEMS+OLD/CT
L41            1 SEA ABB=ON  L30 AND (L38 OR L39 OR L40)

     FILE 'REGISTRY' ENTERED AT 14:42:29 ON 19 MAR 2008
L42              ANALYZE L13 1- LC :       10 TERMS
                 D
L43            2 SEA ABB=ON  L13 AND MEDLINE/LC

     FILE 'MEDLINE' ENTERED AT 14:43:19 ON 19 MAR 2008
L44           79 SEA ABB=ON  L43
                 D TRIAL 1-4
L45           17 SEA ABB=ON  L44 AND PY<2004
L46           27 SEA ABB=ON  KARAOLIS D?/AU
L47            6 SEA ABB=ON  L44 AND L46

     INDEX '1MOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE, AGRICOLA,
     ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE, BABS,
     BIBLIODATA, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA,
     CAOLD, CAPLUS, CASREACT, CBNB, CEABA-VTB, CERAB, ...' ENTERED AT 14:45:54
     ON 19 MAR 2008
                 SEA CYCLIC DI GMP
                 ---------
                11   FILE AGRICOLA
                 5   FILE BIOENG
                44   FILE BIOSIS
                 6   FILE BIOTECHABS
                 6   FILE BIOTECHDS
                 4   FILE BIOTECHNO
                 8   FILE CABA
                40   FILE CAPLUS
```

```
  1   FILE CASREACT
  4   FILE COMPENDEX
 11   FILE CONFSCI
  4   FILE DGENE
  1   FILE DISSABS
  3   FILE EMBAL
  SEA CYCLIC(W) DI(W)((GUANOSINE(W)( MONOPHOSPHATE OR MONOPHOSPHA
 ---------
 12   FILE AGRICOLA
  1   FILE BABS
  6   FILE BIOENG
 49   FILE BIOSIS
  6   FILE BIOTECHABS
  6   FILE BIOTECHDS
  4   FILE BIOTECHNO
  8   FILE CABA
 41   FILE CAPLUS
  1   FILE CASREACT
  5   FILE COMPENDEX
 11   FILE CONFSCI
  4   FILE DGENE
  1   FILE DISSABS
  3   FILE EMBAL
 41   FILE EMBASE
  1   FILE ENERGY
 45   FILE ESBIOBASE
  5   FILE FSTA
 49   FILE GENBANK
  3   FILE IFIPAT
  SEA CYCLIC(W) DI(W)((GUANOSINE(2W)( MONOPHOSPHATE OR MONOPHOSPH
 ---------
 12   FILE AGRICOLA
  1   FILE BABS
  6   FILE BIOENG
 49   FILE BIOSIS
  6   FILE BIOTECHABS
  6   FILE BIOTECHDS
  4   FILE BIOTECHNO
  8   FILE CABA
 41   FILE CAPLUS
  1   FILE CASREACT
  5   FILE COMPENDEX
 11   FILE CONFSCI
  4   FILE DGENE
  1   FILE DISSABS
  3   FILE EMBAL
 41   FILE EMBASE
  1   FILE ENERGY
 45   FILE ESBIOBASE
  5   FILE FSTA
 51   FILE GENBANK
  3   FILE IFIPAT
  6   FILE INPADOCDB
  1   FILE INSPEC
 39   FILE LIFESCI
 49   FILE MEDLINE
 24   FILE PASCAL
 12   FILE PCTFULL
 79   FILE SCISEARCH
  1   FILE SOLIDSTATE
```

```
              8   FILE TOXCENTER
             15   FILE USGENE
             11   FILE USPATFULL
              2   FILE WPIDS
              1   FILE WPIFV
              2   FILE WPINDEX
L48            QUE ABB=ON  CYCLIC(W) DI(W)((GUANOSINE(2W)(MONOPHOSPHATE OR
               MONOPHOSPHATE)) OR GMP)
               ---------
               D RANK

     FILE 'STNGUIDE' ENTERED AT 14:48:58 ON 19 MAR 2008
               D RANK

     FILE 'MEDLINE, AGRICOLA, PASCAL, CABA, WPIX, BIOTECHNO, BIOSIS,
     ESBIOBASE, LIFESCI, CONFSCI, BIOTECHDS, DISSABS, BIOENG, EMBASE' ENTERED
     AT 15:19:37 ON 19 MAR 2008
L49          184 SEA ABB=ON  KARAOLIS D?/AU
L50          298 SEA ABB=ON  CYCLIC(W) DI(W)((GUANOSINE(2W)(MONOPHOSPHATE OR
                 MONO PHOSPHATE)) OR GMP)
L51          117 SEA ABB=ON  CYCLIC(W)(DINUCLEOTIDE OR (DI NUCLEOTIDE))
L52        76606 SEA ABB=ON  BIOFILM# OR BIO FILM#
L53       287453 SEA ABB=ON  VIRULENCE
L54       304524 SEA ABB=ON  COLONIZ? OR COLONIS?
L55       308594 SEA ABB=ON  STAPH? AUREUS
L56        40320 SEA ABB=ON  VIBRIO CHOLERAE
L57        23381 SEA ABB=ON  SALMONELLA ENTERITIDIS
L58      6555431 SEA ABB=ON  INFECT?
L59        61363 SEA ABB=ON  MASTITIS
L60      2139386 SEA ABB=ON  MICROB?
L61       335747 SEA ABB=ON  ANTIMICROB?
L62       445499 SEA ABB=ON  ANTIBACTERI?
L63      5163539 SEA ABB=ON  BACTERI?
L64       881355 SEA ABB=ON  IMPLANT?
L65       390178 SEA ABB=ON  PROSTHE?
L66           30 SEA ABB=ON  L49 AND (L50 OR L51)
L67            8 DUP REM L66 (22 DUPLICATES REMOVED)
                       ANSWERS '1-5' FROM FILE MEDLINE
                       ANSWERS '6-8' FROM FILE WPIX
L68          323 SEA ABB=ON  (L50 OR L51) AND (L52 OR L53 OR L54 OR L55 OR L56
                 OR L57 OR L58 OR L59 OR L60 OR L61 OR L62 OR L63 OR L64 OR
                 L65)
L69          181 SEA ABB=ON  (L50 OR L51) AND (L52 OR L53)
L70          182 SEA ABB=ON  (L50 OR L51) AND (L52 OR L53 OR L54)
L71          161 SEA ABB=ON  L70 NOT L66
L72           38 DUP REM L71 (123 DUPLICATES REMOVED)
                       ANSWERS '1-26' FROM FILE MEDLINE
                       ANSWERS '27-28' FROM FILE PASCAL
                       ANSWER '29' FROM FILE WPIX
                       ANSWERS '30-31' FROM FILE BIOSIS
                       ANSWERS '32-33' FROM FILE ESBIOBASE
                       ANSWER '34' FROM FILE LIFESCI
                       ANSWERS '35-36' FROM FILE CONFSCI
                       ANSWER '37' FROM FILE BIOENG
                       ANSWER '38' FROM FILE EMBASE
L73           30 SEA ABB=ON  L66 OR (L66 AND (L52 OR L53 OR L54 OR L55 OR L56
                 OR L57 OR L58 OR L59 OR L60 OR L61 OR L62 OR L63 OR L64 OR
                 L65))

     FILE 'CAPLUS' ENTERED AT 15:26:34 ON 19 MAR 2008
```

```
L74          41 SEA ABB=ON  CYCLIC/OBI(W) DI/OBI(W)((GUANOSINE/OBI(2W)(MONOPHOS
                PHATE/OBI OR MONO PHOSPHATE/OBI)) OR GMP/OBI)
L75          28 SEA ABB=ON  CYCLIC/OBI(W)(DINUCLEOTIDE/OBI OR (DI NUCLEOTIDE/OB
                I))
L76          39 SEA ABB=ON  (L74 OR L75) AND (L17 OR L18 OR L19 OR L20 OR L21
                OR L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L32 OR L36
                OR L38 OR L39 OR L40)
                D QUE
L77          23 SEA ABB=ON  (L74 OR L75) AND (L23 OR L27 OR L28 OR L36 OR L38
                OR L39 OR L40)
L78          18 SEA ABB=ON  (L74 OR L75) AND (L23 OR L27 OR L28)
L79          17 SEA ABB=ON  L78 NOT (L16 OR L33 OR L35 OR L37 OR L41)
L80          18 SEA ABB=ON  L74(W)PHOSPHODIESTERASE#/OBI
L81          10 SEA ABB=ON  L78 NOT L80
L82           4 SEA ABB=ON  L15 AND (L74 OR L75)

     FILE 'REGISTRY' ENTERED AT 15:30:35 ON 19 MAR 2008
L83             STRUCTURE UPLOADED
L84           3 SEA SUB=L13 SSS SAM L83
L85          58 SEA SUB=L13 SSS FUL L83 EXTEND
L86          40 SEA SUB=L13 SSS FUL L83
                SAVE TEMP L86 ARC591SUB1/A

     FILE 'CAPLUS' ENTERED AT 15:32:11 ON 19 MAR 2008
L87         108 SEA ABB=ON  L86
L88          32 SEA ABB=ON  L30 AND L87
                D QUE NOS L33

     FILE 'STNGUIDE' ENTERED AT 15:33:37 ON 19 MAR 2008

     FILE 'CAPLUS' ENTERED AT 15:34:46 ON 19 MAR 2008
                D QUE NOS L16
                D QUE NOS L82
L89           9 SEA ABB=ON  (L16 OR L82)

     FILE 'MEDLINE' ENTERED AT 15:34:46 ON 19 MAR 2008
                D QUE NOS L45
                D QUE NOS L47

     FILE 'MEDLINE, AGRICOLA, PASCAL, CABA, WPIX, BIOTECHNO, BIOSIS,
     ESBIOBASE, LIFESCI, CONFSCI, BIOTECHDS, DISSABS, BIOENG, EMBASE' ENTERED
     AT 15:35:19 ON 19 MAR 2008
                D QUE L73

     FILE 'CAPLUS, MEDLINE, AGRICOLA, PASCAL, WPIX, BIOSIS, ESBIOBASE,
     LIFESCI, BIOTECHDS, BIOENG, EMBASE' ENTERED AT 15:35:48 ON 19 MAR 2008
L90          12 DUP REM L89 L47 L73 (33 DUPLICATES REMOVED)
                       ANSWERS '1-9' FROM FILE CAPLUS
                       ANSWERS '10-11' FROM FILE MEDLINE
                       ANSWER '12' FROM FILE WPIX
                D IBIB ABS HITIND HITSTR 1-9
                D IALL 10-11
                D IALL ABEX TECH 12

     FILE 'MEDLINE, AGRICOLA, PASCAL, CABA, WPIX, BIOTECHNO, BIOSIS,
     ESBIOBASE, LIFESCI, CONFSCI, BIOTECHDS, DISSABS, BIOENG, EMBASE' ENTERED
     AT 15:36:33 ON 19 MAR 2008
                D QUE L70
L91         161 SEA ABB=ON  L70 NOT L73
```

```
     FILE 'CAPLUS' ENTERED AT 15:36:54 ON 19 MAR 2008

     FILE 'REGISTRY' ENTERED AT 15:36:56 ON 19 MAR 2008
               D STAT QUE L13

     FILE 'CAPLUS' ENTERED AT 15:37:21 ON 19 MAR 2008
               D QUE NOS L33
               D QUE NOS L35
               D QUE NOS L37
               D QUE NOS L41
L92          10 SEA ABB=ON  (L33 OR L35 OR L37 OR L41) NOT (L16 OR L82)

     FILE 'MEDLINE' ENTERED AT 15:37:40 ON 19 MAR 2008
               D QUE NOS L45
L93          17 SEA ABB=ON  L45 NOT L47

     FILE 'CAPLUS, MEDLINE' ENTERED AT 15:37:59 ON 19 MAR 2008
L94          23 DUP REM L92 L93 (4 DUPLICATES REMOVED)
                    ANSWERS '1-10' FROM FILE CAPLUS
                    ANSWERS '11-23' FROM FILE MEDLINE
               D IBIB ABS HITIND HITSTR 1-10
               D IALL 11-23

     FILE 'REGISTRY' ENTERED AT 15:39:42 ON 19 MAR 2008
L95           2 SEA ABB=ON  61093-23-0 OR  73120-97-5
               D IDE 1-2

     FILE 'MEDLINE, AGRICOLA, PASCAL, CABA, WPIX, BIOTECHNO, BIOSIS,
     ESBIOBASE, LIFESCI, CONFSCI, BIOTECHDS, DISSABS, BIOENG, EMBASE' ENTERED
     AT 15:40:36 ON 19 MAR 2008
               D QUE L70
L96         161 SEA ABB=ON  L70 NOT L73

     FILE 'CAPLUS' ENTERED AT 15:40:42 ON 19 MAR 2008
               D QUE L81
L97           9 SEA ABB=ON  L81 NOT (L82 OR L16 OR L92)

     FILE 'CAPLUS, MEDLINE, AGRICOLA, PASCAL, CABA, WPIX, BIOSIS, ESBIOBASE,
     LIFESCI, CONFSCI, BIOTECHDS, BIOENG, EMBASE' ENTERED AT 15:40:49 ON 19
     MAR 2008
L98          39 DUP REM L97 L96 (131 DUPLICATES REMOVED)
                    ANSWERS '1-9' FROM FILE CAPLUS
                    ANSWERS '10-28' FROM FILE MEDLINE
                    ANSWERS '29-30' FROM FILE PASCAL
                    ANSWERS '31-32' FROM FILE BIOSIS
                    ANSWERS '33-34' FROM FILE ESBIOBASE
                    ANSWER '35' FROM FILE LIFESCI
                    ANSWERS '36-37' FROM FILE CONFSCI
                    ANSWER '38' FROM FILE BIOENG
                    ANSWER '39' FROM FILE EMBASE
               D IBIB ABS HITIND 1-9
               D IALL 10-39

     FILE 'STNGUIDE' ENTERED AT 15:41:55 ON 19 MAR 2008
               D COST

     FILE 'REGISTRY' ENTERED AT 15:42:29 ON 19 MAR 2008
               D STAT QUE L86

     FILE 'CAPLUS' ENTERED AT 15:42:36 ON 19 MAR 2008
```

```
                D QUE NOS L88
L99           25 SEA ABB=ON  L88 NOT (L16 OR L92 OR L82 OR L81)
                D IBIB ABS HITSTR L99 1-25

     FILE 'HOME' ENTERED AT 15:43:12 ON 19 MAR 2008
                D STAT QUE L86

=>
```